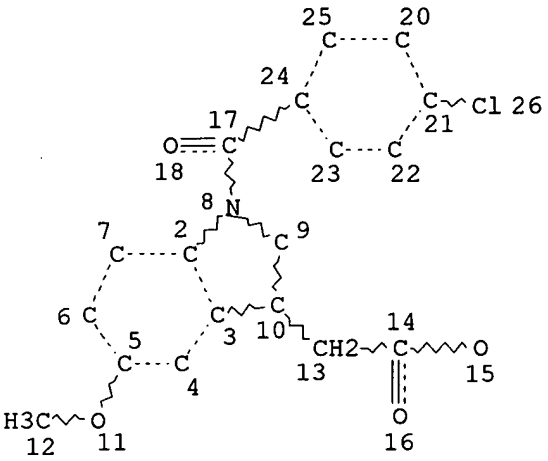
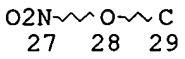
Mitchell G.
09/147770

FILE 'REGISTRY' ENTERED AT 11:07:14 ON 22 APR 2005

L1 STR





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NODE ATTRIBUTES:
NSPEC IS RC AT 29
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE
L2 12 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 60 ITERATIONS 12 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 11:07:43 ON 22 APR 2005
L3 12 S L2

L3 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:64442 CAPLUS
TITLE: Evaluation of the antitumoral potential of different nitric oxide-donating non-steroidal anti-inflammatory drugs (NO-NSAIDs) on human urological tumor cell lines
AUTHOR(S): Huguenin, Sandra; Vacherot, Francis; Fleury-Feith, Jocelyne; Riffaud, Jean-Pierre; Chopin, Dominique K.; Bolla, Manlio; Jaurand, Marie-Claude
CORPORATE SOURCE: Oncogenese des Tumeurs Respiratoires et Urogenitales, Groupe de recherche INSERM E 03-37, Faculte de Medecine, Creteil, 94010, Fr.
SOURCE: Cancer Letters (Amsterdam, Netherlands) (2005), 218(2), 163-170
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Our work aimed at identifying the antitumoral potential of new nitric oxide (NO)-releasing nonsteroidal anti-inflammatory drug (NSAID) derivs. on human prostate and bladder carcinoma cell lines. Among all

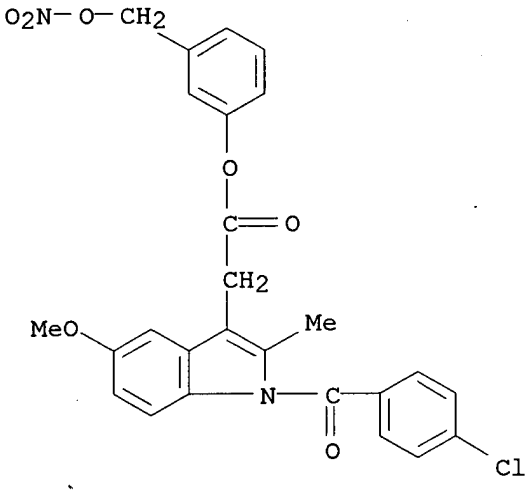
mols. tested, two sulindac derivs., NCX 1102 ((Z)-5-fluoro-2-methyl-1-[[4-(methylsulfinyl)phenyl] methylene]-1H-indene-3-acetic acid 4-(nitrooxy)butyl ester) and NCX 1105 ((Z)-5-fluoro-2-methyl-1-[[4-(methylsulfinyl)phenyl] methylene]-1H-indene-3-acetic acid 6-(nitrooxymethyl)-2-methylpyridyl ester hydrochloride), were the most cytotoxic compds. In contrast to its parent mol. sulindac, cell cycle anal. showed that NCX 1102 led to cell accumulation in the G2-M transition stage in all cell lines, and induced apoptosis in five out of the six cell lines. Thus, NO-NSAIDs may be useful for the elaboration of new therapeutic strategies in the management of bladder and prostate cancer.

IT INDEXING IN PROGRESS

IT **204268-63-3**, NCX 530
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor potential of different nitric oxide-donating non-steroidal anti-inflammatory drugs (NO-NSAIDs) on human urol. tumor cell lines)

RN 204268-63-3 CAPLUS

CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 3-[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:41217 CAPLUS

DOCUMENT NUMBER: 140:111135

TITLE: Preparation of nitrosated nonsteroidal antiinflammatory compounds

INVENTOR(S): Earl, Richard A.; Ezawa, Maiko; Fang, Xinqin; Garvey, David S.; Gaston, Ricky D.; Khanapure, Subhash P.; Letts, Gordon L.; Lin, Chia-En; Ranatunge, Ramani R.; Richardson, Stewart K.; Schroeder, Joseph D.; Stevenson, Cheri A.; Wey, Shiow-Jyi

PATENT ASSIGNEE(S): Nitromed, Inc., USA

SOURCE: PCT Int. Appl., 145 pp.

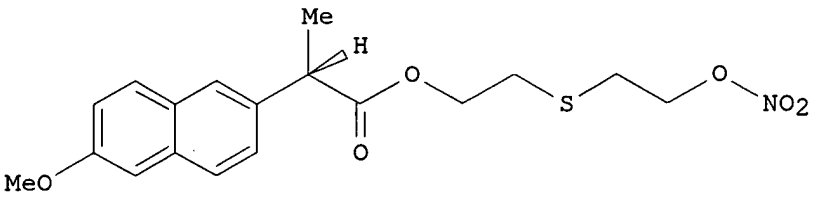
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004648	A2	20040115	WO 2003-US21026	20030703
WO 2004004648	A3	20041028		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004024057	A1	20040205	US 2003-612014		20030703
PRIORITY APPLN. INFO.:			US 2002-393111P	P	20020703
			US 2002-397979P	P	20020724
			US 2002-418353P	P	20021016
			US 2003-449798P	P	20030226
			US 2003-456182P	P	20030321

OTHER SOURCE(S): MARPAT 140:111135
GI



II

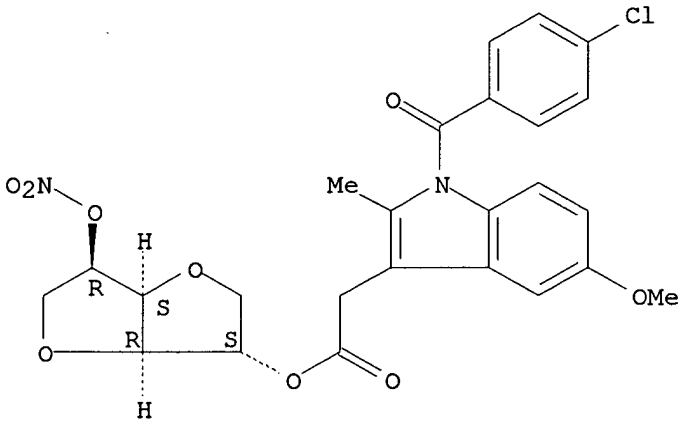
AB Title compds. RnRmHC-CO-X [Rm = H, alkyl; Rn = 4-((thiophen-2-yl)carbonyl)phenyl, 3-(benzoyl)phenyl, etc.; X = Y-alkyl-aryl, etc.; Y = O, S; I] are prepared For instance, naproxen is coupled to 2,2'-thiodiethanol (CH2Cl2, DMAP, EDCI) and treated with Ac2O/HNO3 at 0° to give II. I are nitrosated nonsteroidal antiinflammatory drugs (NSAIDs) used alone or are combined with one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase. The invention provides methods for treating inflammation, pain, fever, gastrointestinal disorders, etc.

IT **646511-22-0P**, [(1S,2S,5S,6R)-6-(Nitrooxy)-4,8-dioxabicyclo[3.3.0]octan-2-yl] 2-[1-[(4-chlorophenyl)carbonyl]-5-

methoxy-2-methylindol-3-yl]acetate **646511-30-0P**,
(2R)-2,3-Bis(nitrooxy)propyl 2-[1-[(4-chlorophenyl)carbonyl]-5-methoxy-2-methylindol-3-yl]acetate **646511-32-2P**,
(2S)-2,3-Bis(nitrooxy)propyl 2-[1-[(4-chlorophenyl)carbonyl]-5-methoxy-2-methylindol-3-yl]acetate **646511-41-3P**,
[N-Methyl-N-[2-(nitrooxy)ethyl]carbamoyl]methyl 2-[1-[(4-chlorophenyl)carbonyl]-5-methoxy-2-methylindol-3-yl]acetate **646511-43-5P**, [N-[2-(Nitrooxy)ethyl]carbamoyl]methyl 2-[1-[(4-chlorophenyl)carbonyl]-5-methoxy-2-methylindol-3-yl]acetate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of naproxen-derived nitrosated antiinflammatory compds.)

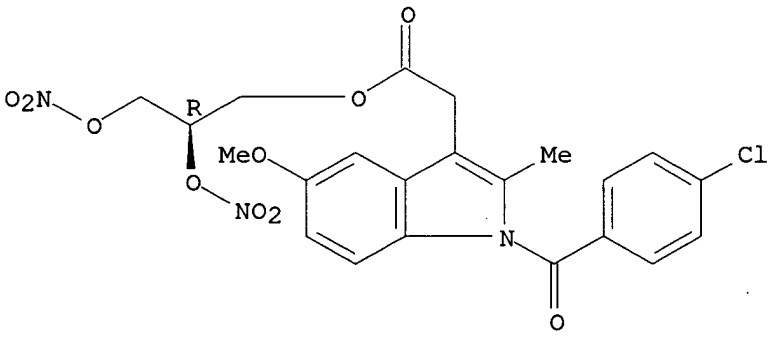
RN 646511-22-0 CAPLUS
CN D-Glucitol, 1,4:3,6-dianhydro-, 2-[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetate] 5-nitrate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



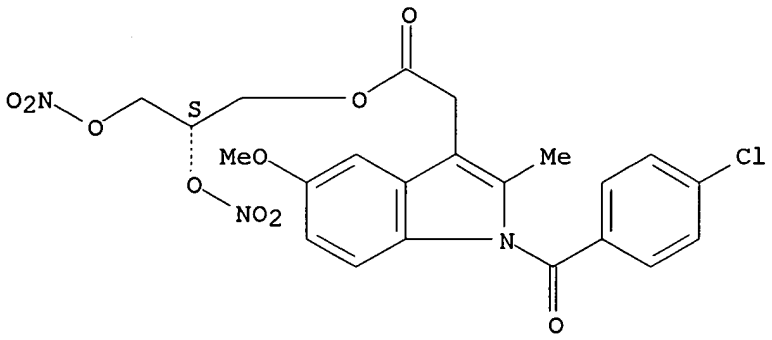
RN 646511-30-0 CAPLUS
CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, (2R)-2,3-bis(nitrooxy)propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

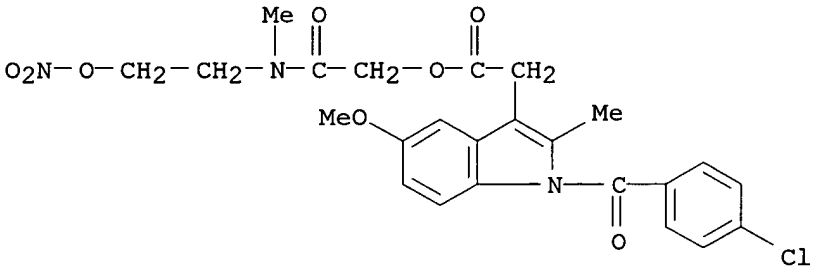


RN 646511-32-2 CAPLUS
CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, (2S)-2,3-bis(nitrooxy)propyl ester (9CI) (CA INDEX NAME)

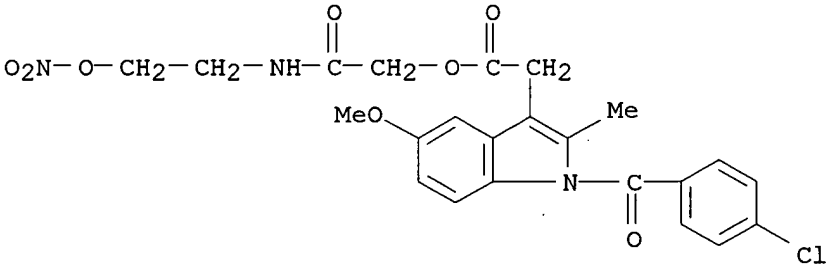
Absolute stereochemistry.



RN 646511-41-3 CAPLUS
CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 2-[methyl[2-(nitrooxy)ethyl]amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)



RN 646511-43-5 CAPLUS
CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 2-[[2-(nitrooxy)ethyl]amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)



L3 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:818296 CAPLUS
DOCUMENT NUMBER: 139:302040
TITLE: Nitrooxy derivatives of antiinflammatory/analgesic compounds for the treatment of arthritis
INVENTOR(S): Del Soldato, Piero

PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084550	A1	20031016	WO 2003-EP3183	20030327
W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, SG, TN, TT, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1492543	A1	20050105	EP 2003-720377	20030327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: IT 2002-MI773 A 20020411
WO 2003-EP3183 W 20030327

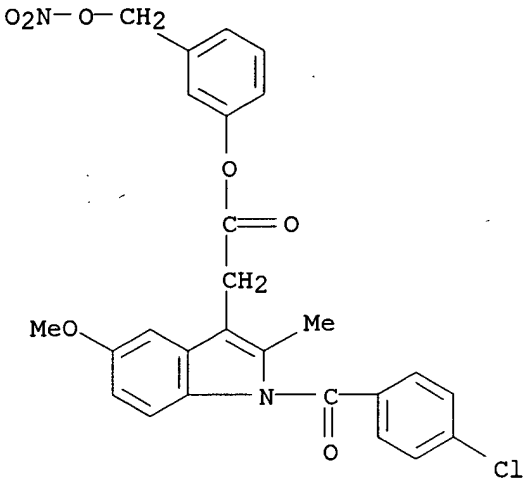
OTHER SOURCE(S): MARPAT 139:302040

AB Antiinflammatory and/or antiinflammatory/analgesic compds. having the formula A(B)b0(C)c0-N(O)s [A contains radical of nonsteroidal antiinflammatory or nonsteroidal antiinflammatory/analgesic drug; B, C = bivalent linking group; s = 1, 2; b0, c0 = 0, 1 (with proviso)], and salts thereof, are disclosed for use in the treatment of arthritis.

IT **204268-63-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

RN 204268-63-3 CAPLUS

CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 3-[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



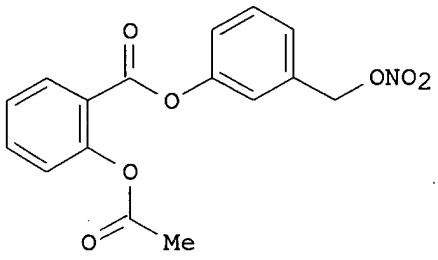
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:293592 CAPLUS
DOCUMENT NUMBER: 136:325420
TITLE: Drugs for diabetes, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030867	A2	20020418	WO 2001-EP11665	20011009
WO 2002030867	A3	20020725		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 1319201	B1	20030926	IT 2000-MI2201	20001012
CA 2425655	AA	20020418	CA 2001-2425655	20011009
AU 2002014006	A5	20020422	AU 2002-14006	20011009
EP 1324974	A2	20030709	EP 2001-982414	20011009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511456	T2	20040415	JP 2002-534256	20011009

US 2004023890 A1 20040205 US 2003-398511 20030411
PRIORITY APPLN. INFO.: IT 2000-MI2201 A 20001012
WO 2001-EP11665 W 20011009

OTHER SOURCE(S): MARPAT 136:325420
GI



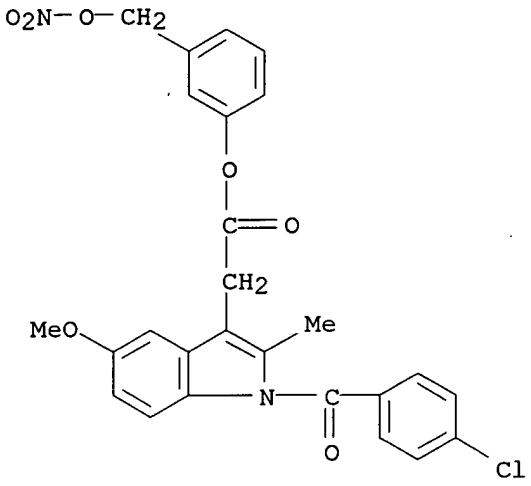
II

AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)n-(C)m-NO2 [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies, neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of . desoxyribose in aqueous Fe2+(NH4)2(SO4)2/thiobarbituric acid solution; and (test 4): inhibition by ≥ 50% of DPPH-induced radical production in MeOH solution For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitation of the resultant Ph ester with HNO3/H2SO4 (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10-4 M gave 70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.

IT **204268-63-3P**, 1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-3-indoleacetic acid 3-(nitroxymethyl)phenyl ester
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(comparison drug candidate; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

RN 204268-63-3 CAPLUS

CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 3-[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



L3 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:659177 CAPLUS
DOCUMENT NUMBER: 136:334926
TITLE: Lack of gastric toxicity of nitric oxide-releasing indomethacin, NCX-530, in experimental animals
AUTHOR(S): Takeuchi, Koji; Mizoguchi, Hiroyuki; Araki, Hideo; Komoike, Yusaku; Suzuki, Keizo
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, Kyoto Pharmaceutical University, Kyoto, 607-8414, Japan
SOURCE: Digestive Diseases and Sciences (2001), 46(8), 1805-1818
CODEN: DDSCDJ; ISSN: 0163-2116
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

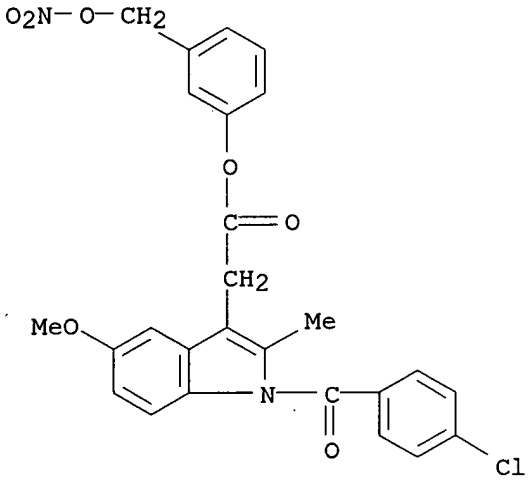
AB The effects of a NO releasing derivative of indomethacin (NCX-530) on gastric ulcerogenic and healing responses were evaluated in rats and mice, in comparison with the parent compound indomethacin. Indomethacin (per os) produced damage in the rat stomach in a dose-dependent manner. NCX-530 (per os) itself, however, was not ulcerogenic and even showed a dose-dependent protection against HCl/EtOH-induced lesions in the rat stomach. Likewise, indomethacin given repeatedly delayed healing of gastric ulcers induced in mice by thermal cauterization, while NCX-530 did not affect the healing response and significantly promoted the healing as compared to indomethacin. These actions of NCX-530 were mimicked by the combined administration of a NO donor NOR-3 with indomethacin. The amount of NO metabolites was increased in both the gastric contents and blood serum when NCX-530, but not indomethacin, was given in pylorus-ligated stomachs. Neither indomethacin nor NCX-530 influenced gastric acid secretion and trans-mucosal p.d., yet NCX-530 caused a marked increase of gastric mucosal blood flow, which was preventable by carboxy-PTIO, a scavenger of NO. Gastric motility was increased by indomethacin but not by NCX-530. In addition, NCX-530 inhibited PGE2 generation in both the

intact and ulcerated gastric mucosa and showed antiinflammatory action on carrageenan-induced rat paw edema, as effectively as indomethacin. These results suggest that unlike indomethacin, NCX-530 caused neither an irritating action on the stomach nor healing impairment effect on the preexisting gastric ulcers, but conferred gastric protection against HCl/EtOH, despite causing cyclooxygenase inhibition and antiinflammatory action, as effectively as indomethacin. This NO-releasing indomethacin, probably by releasing NO, exerts protective influences, such as an increase of gastric mucosal blood flow, that counteract the potential damaging effects of cyclooxygenase inhibition by indomethacin.

IT **204268-63-3**, NCX 530
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gastric protection of NO-releasing indomethacin, NCX-530)

RN 204268-63-3 CAPLUS

CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 3-[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:136240 CAPLUS
DOCUMENT NUMBER: 135:162327
TITLE: Lack of small intestinal ulcerogenecity of nitric oxide-releasing indomethacin, NCX-530, in rats
AUTHOR(S): Mizoguchi, H.; Hase, S.; Tanaka, A.; Takeuchi, K.
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, Kyoto Pharmaceutical University, Kyoto, 607-8414, Japan
SOURCE: Alimentary Pharmacology and Therapeutics (2001), 15(2), 257-267
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

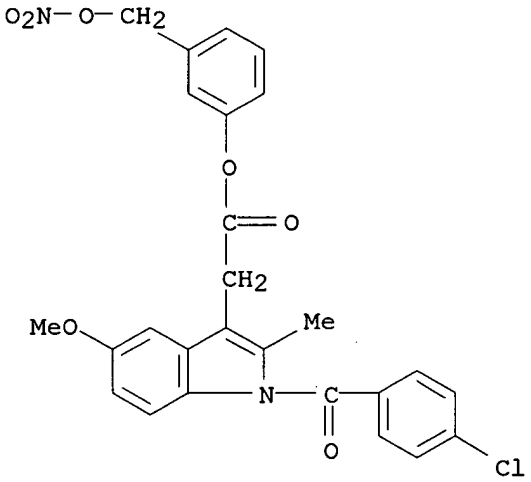
AB Aim: To evaluate the intestinal ulcerogenic property of nitric

oxide-releasing indomethacin (NCX-530) in the rat in comparison with indomethacin. Methods: Animals were given indomethacin or NCX-530 s.c. and killed 24 h later for macroscopic examination of the small intestine. Results: A single administration of indomethacin (10 mg/kg) provoked damage, mainly in the jejunum and ileum, accompanied by an increase in myeloperoxidase and inducible nitric oxide synthase activities as well as bacterial translocation. NCX-530 at an equimolar dose (14.2 mg/kg) caused no gross damage in the small intestine nor any significant change in inducible nitric oxide synthase and myeloperoxidase activities or bacterial translocation. NOR-3, the nitric oxide donor (6.0 mg/kg), when administered s.c. together with indomethacin, significantly prevented the occurrence of intestinal lesions and other mucosal changes. Indomethacin reduced mucus and fluid secretions in the small intestine while both NCX-530 and NOR-3 enhanced these secretions. NCX-530 reduced the mucosal prostaglandin E2 contents and exhibited an anti-inflammatory action against carrageenan-induced paw edema, with equal effectiveness to indomethacin. Conclusion: NCX-530 does not cause intestinal damage, despite inhibiting cyclooxygenase activity. The reduced intestinal toxicity of NCX-530 may be attributable to inhibition of enterobacterial translocation, partly by increasing the mucus and fluid secretions mediated by nitric oxide released from this compound

IT **204268-63-3**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(lack of small intestinal ulcerogenecity of NCX-530 in rats)

RN 204268-63-3 CAPLUS

CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 3-[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:742053 CAPLUS
DOCUMENT NUMBER: 133:310142
TITLE: Synthesis, activity and formulations of

pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.

SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061537	A2	20001019	WO 2000-EP3234	20000411
WO 2000061537	A3	20010927		
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1311924	B1	20020320	IT 1999-MI753	19990413
CA 2370412	AA	20001019	CA 2000-2370412	20000411
BR 2000009702	A	20020108	BR 2000-9702	20000411
EP 1169294	A2	20020109	EP 2000-925203	20000411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541233	T2	20021203	JP 2000-610814	20000411
NZ 514267	A	20040625	NZ 2000-514267	20000411
RU 2237657	C2	20041010	RU 2001-127576	20000411
AU 778989	B2	20041223	AU 2000-44001	20000411
ZA 2001008127	A	20030103	ZA 2001-8127	20011003
NO 2001004927	A	20011213	NO 2001-4927	20011010
US 6869974	B1	20050322	US 2001-926326	20011015

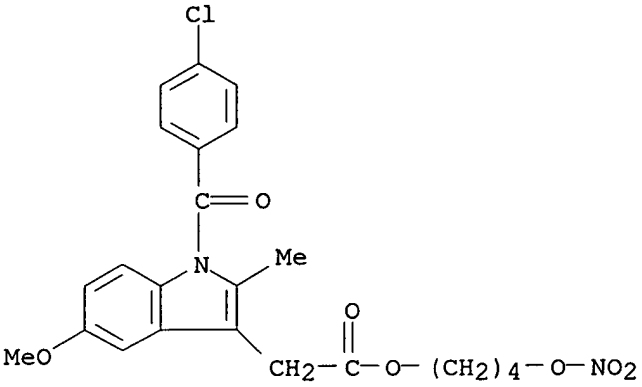
PRIORITY APPLN. INFO.: IT 1999-MI753 A 19990413
WO 2000-EP3234 W 20000411

OTHER SOURCE(S): MARPAT 133:310142

AB Compds. A-B-C-N(O)s and A-C1[N(O)s]-B1 or their salts [s is an integer 1 or 2, preferably s = 2; A is the radical of a drug and is such as to meet the pharmacol. tests reported in the description; C and C1 are two bivalent radicals; the precursors of the radicals B and B1 are such as to meet the pharmacol. test reported in the description] were prepared for use as pharmaceuticals. Thus, (S,S)-N-acetyl-S-(6-methoxy-α-methyl-2-naphthalenylacetyl)cysteine 4-nitroxybutyl ester was prepared (NCX 2101) from naproxene and N-acetylcysteine in the first of 28 synthetic examples given. Pharmacol. test examples and tabular data are also given.

IT **164790-49-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

RN 164790-49-2 CAPLUS
CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



L3 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:628123 CAPLUS
DOCUMENT NUMBER: 133:207818
TITLE: Preparation of nitroxymethylpyridines and related compounds having antiinflammatory, analgesic and antithrombotic activity
INVENTOR(S): Benedini, Francesca; Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051988	A1	20000908	WO 2000-EP1454	20000223
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1308633	B1	20020109	IT 1999-MI413	19990302
CA 2361164	AA	20000908	CA 2000-2361164	20000223
EP 1154999	A1	20011121	EP 2000-909234	20000223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008582	A	20020213	BR 2000-8582	20000223
JP 2002538142	T2	20021112	JP 2000-602215	20000223
AU 770642	B2	20040226	AU 2000-31588	20000223
RU 2240997	C2	20041127	RU 2001-124271	20000223
ZA 2001006650	A	20021113	ZA 2001-6650	20010813
US 6613784	B1	20030902	US 2001-926095	20010830
PRIORITY APPLN. INFO.:			IT 1999-MI413 A	19990302
			WO 2000-EP1454 W	20000223

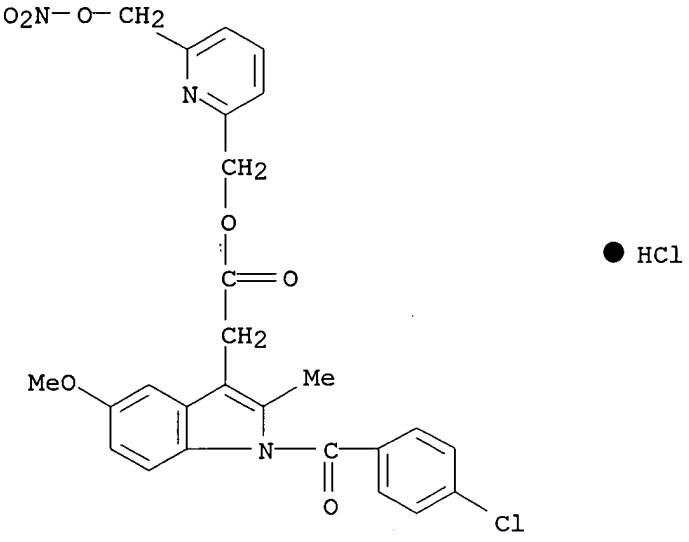
OTHER SOURCE(S): MARPAT 133:207818

AB Organic or inorg. salts of AX1N(O)z [A = R(COXu)t; t = 0, 1; u = 0, 1; X = O, NH, NR1c; R1c = alkyl; R = specified aryl moiety; X1 = (CR1R2)aY(CR3R4)bO; R1-R4 = H, alkyl; a = 0-3; b = 1-3; Y = (aromatic) ring containing ≥1 salifiable N atom], were prepared Thus, 2-acetylbenzoic acid 6-chloromethyl-2-methylpyridinyl ester (preparation given) was heated with AgNO3 in MeCN at 80° for 30 h to give 2-acetylbenzoic acid 6-nitroxymethyl-2-methylpyridinyl ester. The HCl salt of the latter (NCX 4050) at 10-5 M gave 80% inhibition of rabbit aorta contraction.

IT **290335-31-8P 290335-33-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitroxymethylpyridines and related compds. having antiinflammatory, analgesic and antithrombotic activity)

RN 290335-31-8 CAPLUS

CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, [6-[(nitrooxy)methyl]-2-pyridinyl]methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

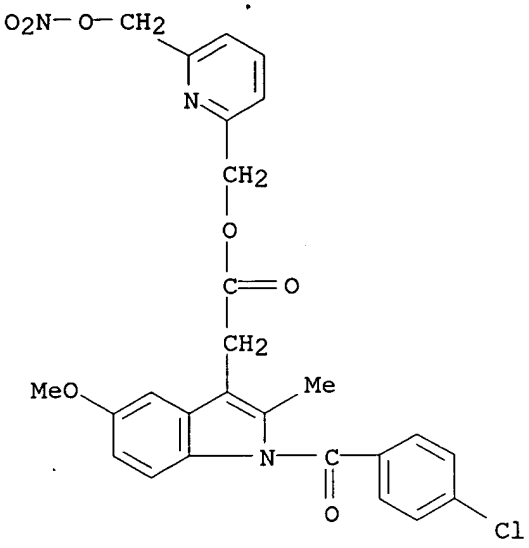


RN 290335-33-0 CAPLUS

CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, [6-[(nitrooxy)methyl]-2-pyridinyl]methyl ester, mononitrate (9CI) (CA INDEX NAME)

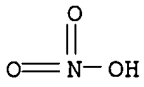
CM 1

CRN 290335-32-9
CMF C26 H22 Cl N3 O7

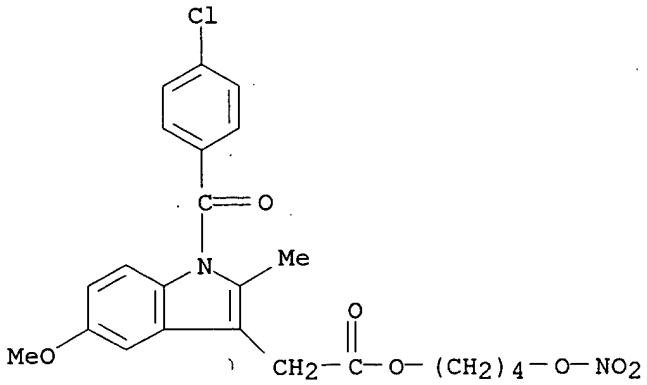


CM 2

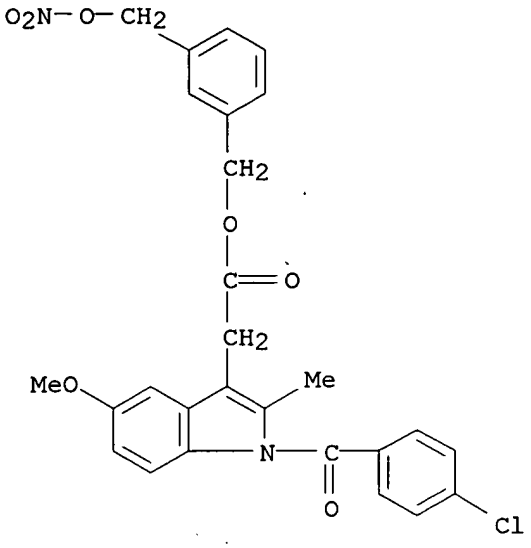
CRN 7697-37-2
CMF H N O3



IT **164790-49-2P 290335-34-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of nitroxymethylpyridines and related compds. having antiinflammatory, analgesic and antithrombotic activity)
RN 164790-49-2 CAPLUS
CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



RN 290335-34-1 CAPLUS
CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, [3-[(nitrooxy)methyl]phenyl]methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:535099 CAPLUS
DOCUMENT NUMBER: 133:152268
TITLE: Synthesis method of (nitroxymethyl)phenyl esters of aspirin derivatives
INVENTOR(S): Del Soldato, Piero; Garufi, Michele
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044705	A1	20000803	WO 2000-EP353	20000118
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1307928	B1	20011129	IT 1999-MI134	19990126
CA 2361454	AA	20000803	CA 2000-2361454	20000118
BR 2000007643	A	20011016	BR 2000-7643	20000118
EP 1147074	A1	20011024	EP 2000-904925	20000118
EP 1147074	B1	20050323		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2002535380	T2	20021022	JP 2000-595962	20000118
AU 766497	B2	20031016	AU 2000-26645	20000118
RU 2232747	C2	20040720	RU 2001-120697	20000118
ZA 2001005705	A	20021011	ZA 2001-5705	20010711
US 6512137	B1	20030128	US 2001-868932	20010717
PRIORITY APPLN. INFO.:			IT 1999-MI134	A 19990126
			WO 2000-EP353	W 20000118

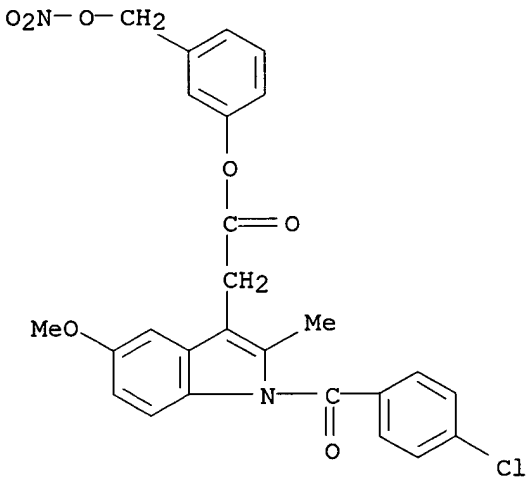
OTHER SOURCE(S): MARPAT 133:152268

AB RCO2H [R = substituted Ph, substituted (phenylcarbonyloxy)phenyl, etc.] were manufactured by (A) esterification of acyl halides RCOX (X = Cl, Br; R as above) with an isomer of hydroxybenzaldehyde in the presence of a base, (B) reduction of aldehyde group of the intermediate ester to give a (hydroxymethyl)phenyl ester, (C) halogenation of the latter ester, e.g., with SOCl2 to obtain the corresponding (chloromethyl)phenyl ester, and (D) reaction of the chlorinated product with an inorg. nitrate salt, e.g., AgNO3. For example, 2-AcOC6H4CO2C6H4(CH2ONO2)-3 was prepared as described above.

IT **204268-63-3P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(manufacture of (nitroxymethyl)phenyl esters of aspirin derivs.)

RN 204268-63-3 CAPLUS

CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 3-[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:221441 CAPLUS

DOCUMENT NUMBER: 128:226234

TITLE: Nonsteroidal anti-inflammatory agents capable of releasing nitric oxide, their preparing method and use

INVENTOR(S): Cai, Xiong; Qian, Changgeng

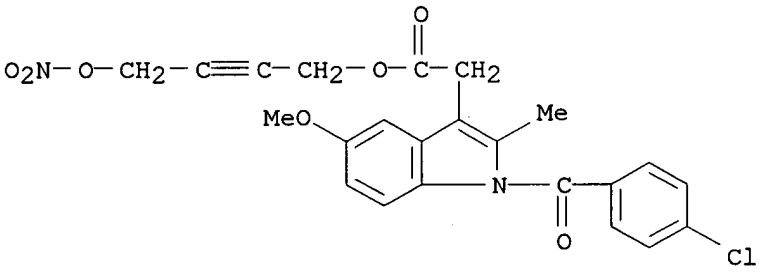
PATENT ASSIGNEE(S): Cai, Xiong, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 22 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1144092	A	19970305	CN 1995-109791	19950825
PRIORITY APPLN. INFO.:			CN 1995-109791	19950825

AB The present invention provides a group of nonsteroidal anti-inflammatory drugs (NSAID) capable of releasing nitric oxide and their nitrates. The NSAID include aspirin, indomethacin, naproxen, brufen, pirprofen, phenol pirprofen, flurbiprofen, ketoprofen, and diclofenac sodium and can be extensively used as antipyretics, analgesics, and antiinflammatory for prevention and treatment of angiocardiopathy and cerebrovascular diseases. The new NSAID nitrates can release nitric oxide in vivo and can reduce the toxicity of NSAID on the digestive tract.

IT **204633-03-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nonsteroidal anti-inflammatory agents capable of releasing nitric oxide, their preparing method and use)

RN 204633-03-4 CAPLUS
CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 4-(nitrooxy)-2-butynyl ester (9CI) (CA INDEX NAME)



L3 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:175910 CAPLUS
DOCUMENT NUMBER: 128:217188
TITLE: Preparation of nitric ester derivatives and their use in urinary incontinence and other diseases
INVENTOR(S): Del Soldato, Piero; Sannicolo', Francesco
PATENT ASSIGNEE(S): Nicox S.A., Fr.; Del Soldato, Piero; Sannicolo', Francesco
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

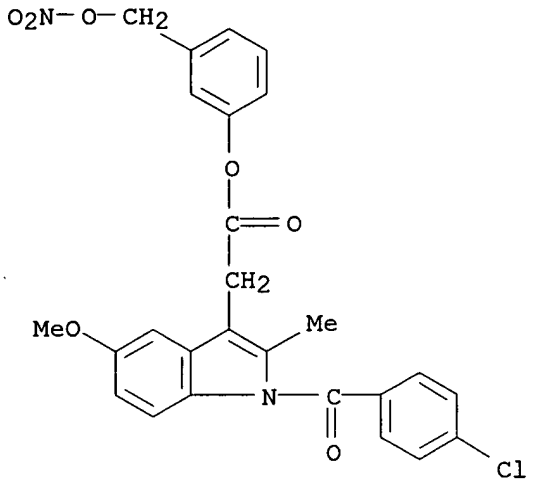
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809948	A2	19980312	WO 1997-EP4774	19970902
WO 9809948	A3	19980604		
W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2264081	AA	19980312	CA 1997-2264081	19970902
AU 9743010	A1	19980326	AU 1997-43010	19970902
AU 729533	B2	20010201		
EP 931065	A2	19990728	EP 1997-919021	19970902
EP 931065	B1	20040728		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, FI, RO				
BR 9712008	A	19990824	BR 1997-12008	19970902
CN 1234792	A	19991110	CN 1997-199130	19970902
JP 2000517332	T2	20001226	JP 1998-512226	19970902
RU 2210563	C2	20030820	RU 1999-106676	19970902
EP 1437132	A1	20040714	EP 2004-101544	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
AT 271858	E	20040815	AT 1997-919021	19970902
EP 1473288	A1	20041103	EP 2004-102724	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, FI, RO				
ES 2224237	T3	20050301	ES 1997-919021	19970902
AU 764127	B2	20030814	AU 2001-38954	20010427
US 2004082652	A1	20040429	US 2003-686907	20031017
PRIORITY APPLN. INFO.:			IT 1996-MI1821	A 19960904
			AU 1997-43010	A3 19970902
			EP 1997-919021	A3 19970902
			WO 1997-EP4774	W 19970902
			US 1999-147770	A3 19990428

OTHER SOURCE(S): MARPAT 128:217188

AB R(COX)tX1NO2 [I; R = e.g., residue of non-steroidal antiinflammatory agent; X = O or (alkyl)imino; X1 = e.g., ZCH2O; Z = 1,3-phenylene], displaying cyclooxygenase inhibiting and myorelaxing effect related to opening of Ca channels and/or release of NO in lower urinary tract, were prepared Thus, flufenamic acid was esterified by 3-(HO)C6H4CH2ONO2 to give 3-(F3C)C6H4NHZ1CO2C6H4(CH2ONO2)-3 (Z1 = 1,2-phenylene). Data for biol. activity of I were given.

IT **204268-63-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitric ester derivs. and their use in urinary

incontinence and other diseases)
RN 204268-63-3 CAPLUS
CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 3-[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



L3 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:667266 CAPLUS
DOCUMENT NUMBER: 123:82961
TITLE: Preparation of organic nitrate esters having antiinflammatory and/or analgesic activity
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox Ltd., Ire.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9509831	A1	19950413	WO 1994-EP3182	19940923
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
GB 2283238	A1	19950503	GB 1993-20599	19931006
GB 2283238	B2	19971126		
CA 2173582	AA	19950413	CA 1994-2173582	19940923
AU 9478092	A1	19950501	AU 1994-78092	19940923
AU 678063	B2	19970515		
EP 722434	A1	19960724	EP 1994-928801	19940923
EP 722434	B1	19980729		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
HU 74446	A2	19961230	HU 1996-874	19940923
HU 218923	B	20001228		

BR 9407749	A	19970212	BR 1994-7749		19940923
JP 09503214	T2	19970331	JP 1994-510585		19940923
AT 168986	E	19980815	AT 1994-928801		19940923
ES 2120070	T3	19981016	ES 1994-928801		19940923
RU 2136653	C1	19990910	RU 1996-108907		19940923
US 5700947	A	19971223	US 1996-624508		19960405
US 5780495	A	19980714	US 1997-902570		19970729
PRIORITY APPLN. INFO.:			GB 1993-20599	A	19931006
			IT 1994-MI916	A	19940510
			WO 1994-EP3182	W	19940923
			US 1996-624508	A3	19960405

OTHER SOURCE(S): CASREACT 123:82961; MARPAT 123:82961

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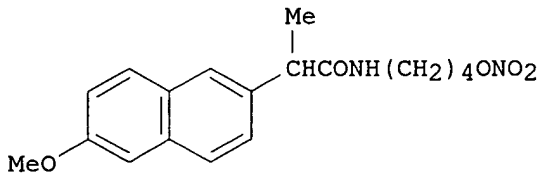

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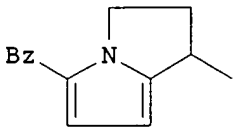

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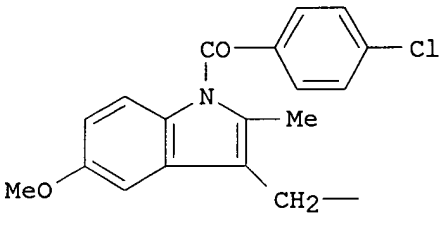
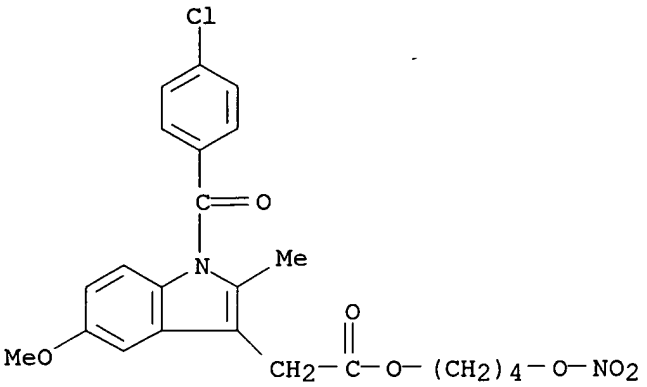


AB The title compds. MCOY[C(A)(B)]nONO2 [A, B = H, (un)branched alkyl; M = Q1, Q2, 2-(6-methoxy)naphthyl, etc.; n = 1-10], useful as analgesics, antiinflammatory agents, and blood platelet aggregation inhibitors, are prepared Thus, 2-(6-methoxy-2-naphthyl)propionic acid was converted into its Na carboxylate salt with NaOEt, the salt condensed with 1-bromo-4-chlorobutane, and the 4-chlorobutyl 2-(6-methoxy-2-naphthyl)propionate intermediate nitrated by reaction with AgNO3, producing the 4-nitratobutyl ester, II.

IT **164790-49-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of organic nitrate esters having antiinflammatory and/or analgesic activity)

RN 164790-49-2 CAPLUS

CN 1H-Indole-3-acetic acid, 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



FILE 'CAOLD' ENTERED AT 11:08:49 ON 22 APR 2005
L4 0 S L2

FILE 'USPATFULL' ENTERED AT 11:08:58 ON 22 APR 2005
L5 9 S L2

L5 ANSWER 1 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2005:71127 USPATFULL
TITLE: Pharmaceutical compounds
INVENTOR(S): Del Soldato, Piero, Milan, ITALY
PATENT ASSIGNEE(S): Nicox S.A., Paris, FRANCE (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6869974	B1	20050322	
	WO 2000061537		20001019	
APPLICATION INFO.:	US 2001-926326		20011015	(9)
	WO 2000-EP3234		20000411	
			20011015	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1999-MI753	19990413

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Raymond, Richard L.
LEGAL REPRESENTATIVE: Arent Fox PLLC
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 2411
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds or their salts having general formulas (I) and (II): wherein s is an integer equal to 1 or 2, A is the radical of a drug that satisfies certain pharmacological tests, C and C.sub.1 are bivalent radicals, and precursors of the radicals B and B.sub.1 satisfy certain pharmacological tests.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2004:108250 USPATFULL

TITLE: Nitric ester derivatives and their use in treating gastrointestinal tumors
INVENTOR(S): Del Soldato, Piero, Monza, ITALY
Sannicolo, Francesco, Milano, ITALY
PATENT ASSIGNEE(S): Nicox S.A. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004082652	A1	20040429
APPLICATION INFO.:	US 2003-686907	A1	20031017 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-147770, filed on 28 Apr 1999, PENDING A 371 of International Ser. No. WO 1997-EP4774, filed on 2 Sep 1997, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1996-MI1821	19960904

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ARENT FOX KINTNER PLOTKIN & KAHN, 1050 CONNECTICUT AVENUE, N.W., SUITE 400, WASHINGTON, DC, 20036
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 1303
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Use of the following groups of compounds or their compositions for the preparation of medicaments for the treatment of gastrointestinal tumors, such compounds having general formula: A-X.sub.1--NO.sub.2 or their salts, where A=R(COX).sub.t and where t is an integer 0 or 1; X.dbd.O, NH, NR.sub.1c, where R.sub.1c is a linear or branched alkyl having from 1 to 10 C atoms; R is (IA) where t=1 and X.sub.1 is equal to --YO-- where Y is a C.sub.1-C.sub.20 alkylene, C.sub.5-C.sub.7 cycloalkyl or oxyalkyl derivatives.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2004:31915 USPATFULL
TITLE: Nitrosated nonsteroidal antiinflammatory compounds, compositions and methods of use related applications
INVENTOR(S): Earl, Richard A., Westford, MA, UNITED STATES
Ezawa, Maiko, Acton, MA, UNITED STATES
Fang, Xinqin, Lexington, MA, UNITED STATES
Garvey, David S., Dover, MA, UNITED STATES
Gaston, Ricky D., Malden, MA, UNITED STATES
Khanapure, Subhash P., Clinton, MA, UNITED STATES
Letts, L. Gordon, Dover, MA, UNITED STATES
Lin, Chia-En, Burlington, MA, UNITED STATES
Ranatunga, Ramani R., Lexington, MA, UNITED STATES
Richardson, Stewart K., Tolland, CT, UNITED STATES
Schroeder, Joseph D., Minneapolis, MN, UNITED STATES
Stevenson, Cheri A., Haverhill, MA, UNITED STATES
Wey, Shiow-Jyi, Woburn, MA, UNITED STATES
PATENT ASSIGNEE(S): NitroMed, Inc. (U.S. corporation)

	NUMBER	KIND	DATE

PATENT INFORMATION:	US 2004024057	A1	20040205
APPLICATION INFO.:	US 2003-612014	A1	20030703 (10)

PRIORITY INFORMATION:	NUMBER	DATE
	US 2002-393111P	20020703 (60)
	US 2002-397979P	20020724 (60)
	US 2002-418353P	20021016 (60)
	US 2003-449798P	20030226 (60)
	US 2003-456182P	20030321 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: EDWARD D GRIEFF, HALE & DORR LLP, 1455 PENNSYLVANIA AVE, NW, WASHINGTON, DC, 20004
NUMBER OF CLAIMS: 58
EXEMPLARY CLAIM: 1
LINE COUNT: 5705
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention describes novel nitrosated nonsteroidal antiinflammatory drugs (NSAIDs) and pharmaceutically acceptable salts thereof, and novel compositions comprising at least one nitrosated NSAID, and, optionally, at least one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase, and/or at least one therapeutic agent. The invention also provides novel compositions comprising at least one nitrosated NSAID, and at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one therapeutic agent. The invention also provides novel kits comprising at least one nitrosated NSAID, and, optionally, at least one nitric oxide donor and/or at least one therapeutic agent. The invention also provides methods for treating inflammation, pain and fever; for treating gastrointestinal disorders; for facilitating wound healing; for treating and/or preventing gastrointestinal, renal and/or respiratory toxicities resulting from the use of nonsteroidal antiinflammatory compounds; for treating inflammatory disease states and/or disorders; and for treating and/or preventing ophthalmic diseases and/or disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 4 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2004:31748 USPATFULL
TITLE: Drugs for diabetes
INVENTOR(S): Del Soldato, Piero, Monza Milano, ITALY

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004023890	A1	20040205
APPLICATION INFO.:	US 2003-398511	A1	20030411 (10)
	WO 2001-EP11665		20011009

PRIORITY INFORMATION:	NUMBER	DATE
	IT 2000-MI2201	20001012

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ARENT FOX KINTNER PLOTKIN & KAHN, 1050 CONNECTICUT AVENUE, N.W., SUITE 400, WASHINGTON, DC, 20036
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 1593
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Use for the diabetes treatment of compounds or salts thereof, having the following general formula (I): A-(B).sub.b0--(C).sub.c0--NO.sub.2 wherein A contains the radical of a drug having an antiiflammatory or analgesic activity, B is a bivalen: linking group wherein the precursor must meet the tests described in the application, C is a a bivalent linking group as defined in the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2003:234795 USPATFULL
TITLE: Nitroxyderivatives having antinflammatory, analgesic and antithrombotic activity
INVENTOR(S): Benedini, Francesca, Milan, ITALY
Del Soldato, Piero, Monza, ITALY
PATENT ASSIGNEE(S): Nicox S.A., Paris, FRANCE (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6613784	B1	20030902	
	WO 2000051988		20000908	
APPLICATION INFO.:	US 2001-926095		20010830	(9)
	WO 2000-EP1454		20000223	

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1999-MI413	19990302

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Davis, Zinna Northington
LEGAL REPRESENTATIVE: Arent Fox Kintner Plotkin & Kahn PLLC
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1127
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Organic or inorganic salts of compounds of general formula: A--X.sub.1--N(O).sub.z for use as medicaments having anti-inflammatory, analgesic and antithrombotic activity, wherein A is R(COX.sub.u).sub.t wherein t is 0 or 1; u is 0 or 1 and X is O, NH, NR.sub.1c wherein R.sub.1c us a C.sub.1-C.sub.10 alkyl and R is, for example, (Ia) wherein R.sub.1 is acetoxy, preferably in ortho position with respect to --CO-- and R.sub.2 is hydrogen or acetylsalicylsalicylic acid derivatives; and X.sub.1 is the formula (B), Y being a ring containing at least one salified nitrogen atom.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 6 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2003:26442 USPATFULL
TITLE: Synthesis method of nitroxymethylphenyl esters of

aspirin derivatives
INVENTOR(S): Del Soldato, Piero, Milan, ITALY
Garufi, Michele, Milan, ITALY
PATENT ASSIGNEE(S): Nicox S.A., Paris, FRANCE (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6512137	B1	20030128	
	WO 2000044705		20000803	
APPLICATION INFO.:	US 2001-868932		20010717	(9)
	WO 2000-EP353		20000118	

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1999-MI134	19990126

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Lambkin, Deborah C.
LEGAL REPRESENTATIVE: Arent Fox Kintner, Plotkin & Kahn PLLC
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 331
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention describes a method for the synthesis of nitroxymethylphenyl esters of aspirin derivatives.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 7 OF 9 USPATFULL on STN
ACCESSION NUMBER: 1999:7413 USPATFULL
TITLE: Nitro compounds of the formula A-X.sub.i -NO.sub.2 and their compositions having anti-inflammatory, analgesic and anti-thrombotic activities
INVENTOR(S): Del Soldato, Piero, Milan, Italy
Sannicolo, Francesco, Milan, Italy
PATENT ASSIGNEE(S): Nicox S.A., Paris, France (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5861426		19990119	
	WO 9530641		19951116	
APPLICATION INFO.:	US 1997-737426		19970306	(8)
	WO 1995-EP1233		19950404	
			19970306	PCT 371 date
			19970306	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1994-MI916	19940510
	IT 1994-MI1731	19940809

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Higel, Floyd D.
LEGAL REPRESENTATIVE: Hale and Dorr LLP
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
LINE COUNT: 1242
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB New compounds and their compositions having anti-inflammatory, analgesic and anti-thrombotic activities, of the general formula: A--X.sub.1 --NO.sub.2 or their salts, wherein: A is R(COX.sub.u).sub.t, wherein t is zero or 1 and u is zero or 1; and X is O, NH or NR.sub.1C wherein R.sub.1C is C.sub.1 -C.sub.10 alkyl; and R is(Ia) wherein R.sub.1 is acetoxoy, preferably n ortho-position with respect to --CO-- and R.sub.2 is hydrogen; or derivatives of acetylsalylsalicyclic acid; and X.sub.1 is --YO-- wherein Y is C.sub.1 -C.sub.20 alkylene, C.sub.5 -C.sub.7 cycloalkylene, oxy-alkyl derivatives and oxy-methyl benzyl derivatives.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 8 OF 9 USPATFULL on STN
ACCESSION NUMBER: 1998:82781 USPATFULL
TITLE: Nitric esters having anti-inflammatory and/or analgesic activity and process for their preparation
INVENTOR(S): Del Soldato, Piero, Milan, Italy
PATENT ASSIGNEE(S): Nicox S.A., Paris, France (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5780495		19980714
APPLICATION INFO.:	US 1997-902570		19970729 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1996-624508, filed on 5 Apr 1996, now patented, Pat. No. US 5700947

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1993-20599	19931006
	IT 1994-MI916	19940510

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: McKane, Joseph
LEGAL REPRESENTATIVE: Hale and Dorr LLP
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
LINE COUNT: 499
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention is directed to nitric esters of derivatives of propionic acid, 1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetic acid, 5-benzoyl-1,2-dihidro-3H-pyrrolo [1,2-a]pyrrole-1-carboxylic acid, 6-methoxy-2-napthylacetic acid, characterized in that they have the following general formula: ##STR1## These nitric ester derivatives may be formulated into pharmaceutical compositions and administered for their anti-inflammatory and/or analgesic activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 9 OF 9 USPATFULL on STN
ACCESSION NUMBER: 97:120757 USPATFULL
TITLE: Nitric esters having anti-inflammatory and/or analgesic activity and process for their preparation
INVENTOR(S): Soldato, Piero Del, Monza, Italy
PATENT ASSIGNEE(S): NICOX S.A., Paris, France (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5700947		19971223	
	WO 9509831		19950413	
APPLICATION INFO.:	US 1996-624508		19960405	(8)
	WO 1994-EP3182		19940923	
			19960405	PCT 371 date
			19960405	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1993-20599	19931006
	IT 1994-MI916	19940510

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Shah, Mukund J.
ASSISTANT EXAMINER: Bucknum, Michael
LEGAL REPRESENTATIVE: Hale and Dorr LLP
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 518
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention is directed to nitric esters of derivatives of propionic acid, 1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetic acid, 5-benzoyl-1,2-dihydro-3H-pyrrolo[1,2-a]pyrrole-1-carboxylic acid, 6-methoxy-2-napthylacetic acid, characterized in that they have the following general formula: ##STR1## These nitric ester derivatives may be formulated into pharmaceutical compositions and administered for their anti-inflammatory and/or analgesic activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 11:09:23 ON 22 APR 2005)
L6 3 S L2
L7 3 DUP REM L6 (0 DUPLICATES REMOVED)

L7 ANSWER 1 OF 3 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:630194 BIOSIS
DOCUMENT NUMBER: PREV200200630194
TITLE: Chemoprevention of colonic aberrant crypt foci by nitric oxide (NO)-releasing NSAIDs.
AUTHOR(S): Rao, Chintalapally V. [Reprint author]; Simi, Barbara; Cooma, Indranie; Rigas, Basil; Kopelovich, Levy; Reddy, Bandaru S.
CORPORATE SOURCE: American Health Foundation, Valhalla, NY, USA
SOURCE: Cancer Epidemiology Biomarkers and Prevention, (October, 2002) Vol. 11, No. 10 Part 2, pp. 1231s. print.
Meeting Info.: Proceedings of the American Association for Cancer Research Conference on Frontiers in Cancer Prevention Research. Boston, MA, USA. October 14-18, 2002. American Society of Preventive Oncology.
ISSN: 1055-9965.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English

Searcher : Shears 571-272-2528

ENTRY DATE: Entered STN: 12 Dec 2002
Last Updated on STN: 20 Jan 2003

L7 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:435900 BIOSIS
DOCUMENT NUMBER: PREV200100435900
TITLE: Lack of gastric toxicity of nitric oxide-releasing indomethacin, NCX-530, in experimental animals.
AUTHOR(S): Takeuchi, Koji [Reprint author]; Mizoguchi, Hiroyuki; Araki, Hideo; Komoike, Yusaku; Suzuki, Keizo
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto, 607-8414, Japan
SOURCE: Digestive Diseases and Sciences, (August, 2001) Vol. 46, No. 8, pp. 1805-1818. print.
CODEN: DDSCDJ. ISSN: 0163-2116.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Sep 2001
Last Updated on STN: 23 Feb 2002

AB The effects of a nitric oxide (NO) releasing derivative of indomethacin (NCX-530) on gastric ulcerogenic and healing responses were evaluated in rats and mice, in comparison with the parent compound indomethacin. Indomethacin (per os) produced damage in the rat stomach in a dose-dependent manner. NCX-530 (per os) itself, however, was not ulcerogenic and even showed a dose-dependent protection against HCl/ethanol-induced lesions in the rat stomach. Likewise, indomethacin given repeatedly delayed healing of gastric ulcers induced in mice by thermal cauterization, while NCX-530 did not affect the healing response and significantly promoted the healing as compared to indomethacin. These actions of NCX-530 were mimicked by the combined administration of a NO donor NOR-3 with indomethacin. The amount of NO metabolites was increased in both the gastric contents and serum when NCX-530, but not indomethacin, was given in pylorus-ligated stomachs. Neither indomethacin nor NCX-530 influenced gastric acid secretion and transmucosal potential difference, yet NCX-530 caused a marked increase of gastric mucosal blood flow, which was preventable by carboxy-PTIO, a scavenger of NO. Gastric motility was increased by indomethacin but not by NCX-530. In addition, NCX-530 inhibited PGE2 generation in both the intact and ulcerated gastric mucosa and showed antiinflammatory action on carrageenan-induced rat paw edema, as effectively as indomethacin. These results suggest that unlike indomethacin, NCX-530 caused neither an irritating action on the stomach nor healing impairment effect on the preexisting gastric ulcers, but conferred gastric protection against HCl/ethanol, despite causing cyclooxygenase inhibition and antiinflammatory action, as effectively as indomethacin. This NO-releasing indomethacin, probably by releasing NO, exerts protective influences, such as an increase of gastric mucosal blood flow, that counteract the potential damaging effects of cyclooxygenase inhibition by indomethacin.

L7 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:122852 BIOSIS
DOCUMENT NUMBER: PREV200100122852
TITLE: Lack of small intestinal ulcerogenecity of nitric oxide-releasing indomethacin, NCX-530, in rats.

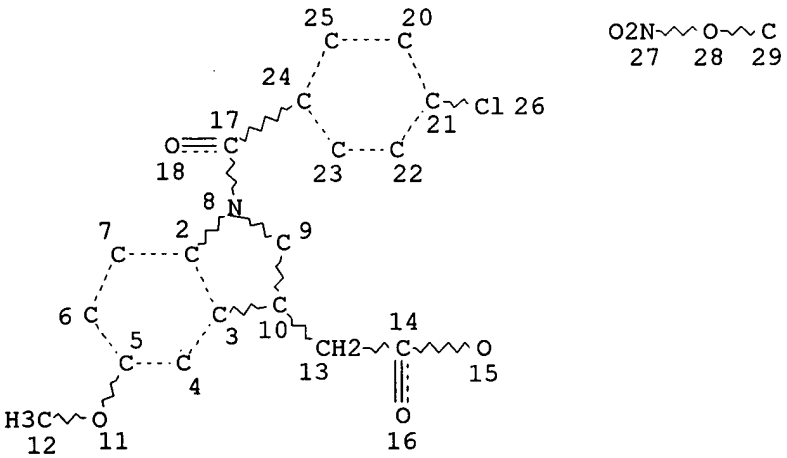
Searcher : Shears 571-272-2528

AUTHOR(S): Mizoguchi, H.; Hase, S.; Tanaka, A.; Takeuchi, K. [Reprint author]
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto, 607-8414, Japan takeuchi@mb.kyoto-phu.ac.jp
SOURCE: Alimentary Pharmacology and Therapeutics, (February, 2001) Vol. 15, No. 2, pp. 257-267. print.
CODEN: APTHEN. ISSN: 0269-2813.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Mar 2001
Last Updated on STN: 15 Feb 2002

AB Aim: To evaluate the intestinal ulcerogenic property of nitric oxide-releasing indomethacin (NCX-530) in the rat, in comparison with indomethacin. Methods: Animals were given indomethacin or NCX-530 subcutaneously and killed 24 h later for macroscopic examination of the small intestine. Results: A single administration of indomethacin (10 mg/kg) provoked damage, mainly in the jejunum and ileum, accompanied by an increase in myeloperoxidase and inducible nitric oxide synthase activities as well as bacterial translocation. NCX-530 at an equimolar dose (14.2 mg/kg) caused no gross damage in the small intestine, nor any significant change in inducible nitric oxide synthase and myeloperoxidase activities or bacterial translocation. NOR-3, the nitric oxide donor (6.0 mg/kg), when administered subcutaneously together with indomethacin, significantly prevented the occurrence of intestinal lesions and other mucosal changes. Indomethacin reduced mucus and fluid secretions in the small intestine, while both NCX-530 and NOR-3 enhanced these secretions. NCX-530 reduced the mucosal prostaglandin E2 contents and exhibited an anti-inflammatory action against carrageenan-induced paw oedema, with equal effectiveness to indomethacin. Conclusion: NCX-530 does not cause intestinal damage, despite inhibiting cyclooxygenase activity. The reduced intestinal toxicity of NCX-530 may be attributable to inhibition of enterobacterial translocation, partly by increasing the mucus and fluid secretions mediated by nitric oxide released from this compound.

(FILE 'MARPAT' ENTERED AT 11:12:04 ON 22 APR 2005)

L1 STR



NODE ATTRIBUTES:

Searcher : Shears 571-272-2528

NSPEC IS RC AT 29
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L9 19 SEA FILE=MARPAT SSS FUL L1 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 177 ITERATIONS 19 ANSWERS
SEARCH TIME: 00.00.01

L9 ANSWER 1 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:350593 MARPAT
TITLE: Use of NO-donating NSAIDs for the treatment of conditions associated with gastrointestinal motility
INVENTOR(S): Jonzon, Bror; Hoogstraate, Janet
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035042	A1	20040429	WO 2003-SE1603	20031015

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 2002-3093 20021018

AB The invention discloses the use of NO-donating nonsteroidal antiinflammatory drugs in the treatment of conditions associated with gastrointestinal motility, a method of treatment of such conditions, and the use of pharmaceutical compns. comprising one or more NO-donating NSAID(s) in the treatment of such conditions. More particularly, the invention is directed to the use of one or more NO-donating NSAID(s) for the manufacture of a medicament for the treatment of conditions associated with disturbed gastrointestinal motility.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 2 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:287165 MARPAT
TITLE: Manufacturing process for NO-donating compounds such as NO-donating diclofenac
INVENTOR(S): Andersson, Johan; Belli, Aldo; Cannata, Vincenzo; Hedberg, Martin; Palmgren, Andreas; Schuldei, Sigrid; Stroem, Marika; Villa, Marco
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Astrazeneca AB
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026808	A1	20040401	WO 2003-SE1465	20030918

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 2002-2801 20020920
SE 2003-1476 20030520
OTHER SOURCE(S): CASREACT 140:287165
AB NO-Donating compds. MLnAmCO2XONOp [M = residue of an NSAID, COX-1 inhibitor or COX-2 inhibitor; L = O, S, CO2, (un)substituted CONH, NH, CO, CH2, CH2CO, CH2CONH, CH2CO2; A = (un)substituted alkylene; X = carbon linker; m, n = 0-3; p= 1, 2] are prepared by treating MLnAmCO2H with HOXOH, treating MLnAmCO2XOH with RSO2Cl [R = alkyl, (un)substituted Ph, CH2Ph, halogen, CF3, C4F9], and treating MLnAmCO2XO3SR with nitrate. A substantially crystalline form of 2-[2-(nitrooxy)ethoxy]ethyl {2-[(2,6-dichlorophenyl)amino]phenyl}aceta te is reported.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:253345 MARPAT
TITLE: Process for preparing nitrooxyalkyl esters of carboxylic acids
INVENTOR(S): Del Soldato, Piero; Santus, Giancarlo; Benedini, Francesca
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020385	A1	20040311	WO 2003-EP8700	20030806

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2002-MI1861 20020829
OTHER SOURCE(S): CASREACT 140:253345
AB RCO2(CR1R2)m(CR3R4)n(CR5R6)oXp(CR7R8)q(CR9R10)r(CR11R12)sONO2 [R = residue of a pharmaceutically active compound, ferulic acid; R1-R12 = H, alkyl, aralkyl; m, n, o, q, r, s = 0-6; p = 0, 1; X = O, S, SO, SO2, NR13, PR13, (substituted) cycloalkylene, arylene, heterocyclylene; R13 = H, alkyl], were prepared by reaction of RCO2Z (R as defined above; Z = H, Li+, Na+, K+, Ca++, Mg++, tetralkylammonium, tetralkylphosphonium) with Y(CR1R2)m(CR3R4)n(CR5R6)oXp(CR7R8)q(CR9R10)r(CR11R12)sONO2 [Y = Br, Cl, iodo, BF4, SbF6, FSO3, ASO3; A = (substituted) alkyl; other variables as defined above]. Thus, ferulic acid, 4-nitrooxybutyl bromide, and Et3N were stirred 3 days in DMF to give 65% ferulic acid 4-nitrooxybutyl ester.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:111135 MARPAT
TITLE: Preparation of nitrosated nonsteroidal antiinflammatory compounds
INVENTOR(S): Earl, Richard A.; Ezawa, Maiko; Fang, Xinqin; Garvey, David S.; Gaston, Ricky D.; Khanapure, Subhash P.; Letts, Gordon L.; Lin, Chia-En; Ranatunge, Ramani R.; Richardson, Stewart K.; Schroeder, Joseph D.; Stevenson, Cheri A.; Wey, Shiow-Jyi
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004648	A2	20040115	WO 2003-US21026	20030703
WO 2004004648	A3	20041028		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

US 2004024057	A1	20040205	US 2003-612014 20030703
PRIORITY APPLN. INFO.:			US 2002-393111P 20020703
			US 2002-397979P 20020724
			US 2002-418353P 20021016
			US 2003-449798P 20030226
			US 2003-456182P 20030321

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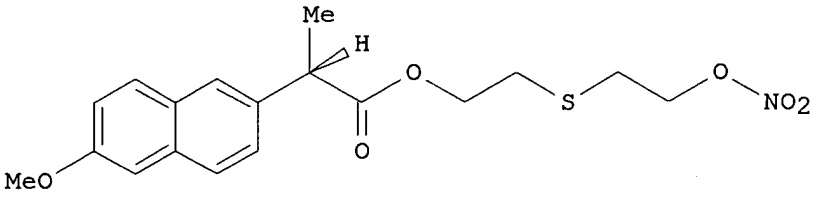

II

AB Title compds. RnRmHC-CO-X [Rm = H, alkyl; Rn = 4-((thiophen-2-yl)carbonyl)phenyl, 3-(benzoyl)phenyl, etc.; X = Y-alkyl-aryl, etc.; Y = O, S; I] are prepared For instance, naproxen is coupled to 2,2'-thiodiethanol (CH2Cl2, DMAP, EDCI) and treated with Ac2O/HNO3 at 0° to give II. I are nitrosated nonsteroidal antiinflammatory drugs (NSAIDs) used alone or are combined with one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase. The invention provides methods for treating inflammation, pain, fever, gastrointestinal disorders, etc.

L9 ANSWER 5 OF 19 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	140:73178 MARPAT
TITLE:	Nitroxy derivatives of non-steroidal anti-inflammatory compounds as selective inhibitors of cyclooxygenase-2 for the treatment of inflammation
INVENTOR(S):	Del Soldato, Piero; Santus, Giancarlo
PATENT ASSIGNEE(S):	Nicox S.A., Fr.
SOURCE:	PCT Int. Appl., 49 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000300	A1	20031231	WO 2003-EP6651	20030624

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2002-MI1399 20020625

AB The present invention relates to compds. able to inhibit selectively the enzyme cyclooxygenase-2 (COX-2) without inhibiting substantially the enzyme COX-1. Specifically, the present invention concerns nitroxy derivs. of non-steroidal anti-inflammatory compds., which are able to inhibit selectively the enzyme COX-2. The compds. of the invention are useful in the treatment and/or prophylaxis of inflammatory processes.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 19 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 139:302040 MARPAT

TITLE: Nitrooxy derivatives of antiinflammatory/analgesic compounds for the treatment of arthritis

INVENTOR(S): Del Soldato, Piero

PATENT ASSIGNEE(S): Nicox S.A., Fr.

SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084550	A1	20031016	WO 2003-EP3183	20030327

W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, SG, TN, TT, UA, US, UZ, VN, YU, ZA

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1492543	A1	20050105	EP 2003-720377	20030327

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: IT 2002-MI773 20020411
WO 2003-EP3183 20030327

AB Antiinflammatory and/or antiinflammatory/analgesic compds. having the formula A(B)b0(C)c0-N(O)s [A contains radical of nonsteroidal antiinflammatory or nonsteroidal antiinflammatory/analgesic drug; B, C = bivalent linking group; s = 1, 2; b0, c0 = 0, 1 (with proviso)], and salts thereof, are disclosed for use in the treatment of arthritis.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR

THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:260440 MARPAT
TITLE: Self emulsifying drug delivery system containing NSAIDs
INVENTOR(S): Holmberg, Christina
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022249	A1	20030320	WO 2002-SE1598	20020905
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1427392	A1	20040616	EP 2002-765747	20020905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005504788	T2	20050217	JP 2003-526379	20020905
US 2004248974	A1	20041209	US 2004-488585	20040304
PRIORITY APPLN. INFO.:			SE 2001-2993	20010907
			WO 2002-SE1598	20020905

AB A pharmaceutical composition suitable for oral administration, in form of an emulsion pre-concentrate, comprises 1 or more NO-releasing NSAID(s), 1 or more surfactants, of which at least one is phospholipid, the composition forming an in-situ oil-in-water emulsion upon contact with gastrointestinal fluids. The composition may optionally also comprise an addnl. oil or semi-solid fat. Further, 1 or more short-chain alcs. can optionally be included in the composition Also within the scope of the invention is a combination with a proton pump inhibitor. The pharmaceutical composition is useful in the treatment of pain and inflammation. Further within the scope of the invention is kit comprising a pharmaceutical composition according to the invention in a unit dosage form, in combination with a proton pump inhibitor, and the proton pump inhibitor is enteric coated. Thus, a formulation contained Lipoid S100 0.30, propylene glycol 0.90, and a NO-releasing NSAID 4.00 g.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:369833 MARPAT
TITLE: Preparation of nitrooxy cysteine derivatives for

the Alzheimer's disease
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092072	A2	20021121	WO 2002-EP5165	20020510
WO 2002092072	A3	20030501		

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2001-MI985 20010515
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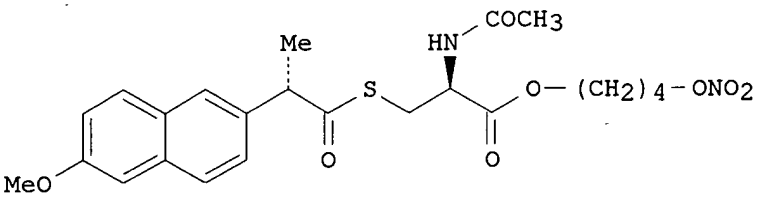

II

AB Title compds. A-Bn-Cm-NO2 [n, m = 0-1 with the proviso that m, n cannot be contemporaneously equal to 0; A = R-T1; R = (hetero)cycle; T1 = (CO)0-1, X0-1; X = O, S, amino; B = T2-X2-T3; T2-3 = CO, X, etc.; X2 = bivalent linking group; C = bivalent linking radical; I] were prepared For instance, 6-methoxy-α-methyl-2-naphthalenacetic acid was coupled to (S)-N-acetylcysteine (DMF/CHCl3, CDI, 12 h), the product converted to the 4-bromobutyl ester (THF, Ph3P, CBr4, 24 h) and that intermediate treated with AgNO3 (CH3CN, reflux, 7 h) to afford II. Nitrooxy derivs. of the invention are effective in inhibiting LPS-induced neurodegeneration and are useful in the treatment of Alzheimer's disease.

L9 ANSWER 9 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:253012 MARPAT
TITLE: Pharmaceutical compositions containing NO-releasing NSAID and surfactants
INVENTOR(S): Siekmann, Britta; Thoring, Barbro
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002074282	A1	20020926	WO 2002-SE476	20020313
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2435825	AA	20020926	CA 2002-2435825	20020313
EP 1370239	A1	20031217	EP 2002-704035	20020313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002007760	A	20040601	BR 2002-7760	20020313
JP 2004523577	T2	20040805	JP 2002-572990	20020313
US 2004096494	A1	20040520	US 2003-471378	20030909
NO 2003004026	A	20031111	NO 2003-4026	20030911
PRIORITY APPLN. INFO.:			SE 2001-901	20010315
			WO 2002-SE476	20020313

AB A new pharmaceutical composition in the form of lipoglobules comprises (a) 1 or more NO-releasing NSAIDs; (b) 1 or more surfactants; and (c) an aqueous phase, and is useful for the treatment of pain and inflammation. Thus, a composition contained 4-(nitrooxy)butyl 6-methoxy-α-methyl-2-naphthaleneacetate 0.77, fractionated coconut oil 2.97, Phospholipon-80 0.76, and Poloxamer-407 1.61 mg/g.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 136:325420 MARPAT
TITLE: Drugs for diabetes, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030867	A2	20020418	WO 2001-EP11665	20011009
WO 2002030867	A3	20020725		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IT 1319201	B1	20030926	IT 2000-MI2201	20001012
CA 2425655	AA	20020418	CA 2001-2425655	20011009
AU 2002014006	A5	20020422	AU 2002-14006	20011009
EP 1324974	A2	20030709	EP 2001-982414	20011009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511456	T2	20040415	JP 2002-534256	20011009
US 2004023890	A1	20040205	US 2003-398511	20030411
PRIORITY APPLN. INFO.:			IT 2000-MI2201	20001012
			WO 2001-EP11665	20011009

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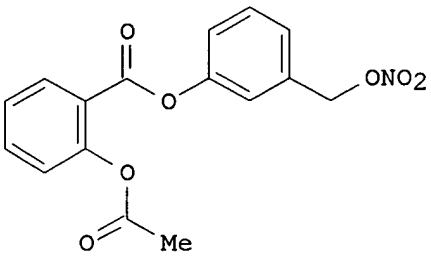

II

AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)n-(C)m-NO2 [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies, neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of . desoxyribose in aqueous Fe2+(NH4)2(SO4)2/thiobarbituric acid solution; and (test 4): inhibition by ≥ 50% of DPPH-induced radical production in MeOH solution For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitation of the resultant Ph ester with HNO3/H2SO4 (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10-4 M gave 70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.

L9 ANSWER 11 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 136:189342 MARPAT
TITLE: Drugs for treatment of sexual dysfunction
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011706	A2	20020214	WO 2001-EP8733	20010727
WO 2002011706	A3	20030918		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 1318673	B1	20030827	IT 2000-MI1847	20000808
AU 2001091690	A5	20020218	AU 2001-91690	20010727
EP 1363628	A2	20031126	EP 2001-971797	20010727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR				
JP 2004506619	T2	20040304	JP 2002-517043	20010727
US 2003171393	A1	20030911	US 2003-333927	20030204
PRIORITY APPLN. INFO.:			IT 2000-MI1847	20000808
			WO 2001-EP8733	20010727

AB Pharmaceuticals containing nitric oxide-donor drugs or inorg. salts of compds. inhibiting phosphodiesterases are useful for the treatment of sexual dysfunction. Thus, a formulation contained 2-(acetyloxy)benzoic acid 6-(nitroxy-methyl)-2-methylpyridyl ester-HCl (NCX 4050) 4.2, white petrolatum 24, Polysorbate-60 4.8, glycerin 9.5, and water 48 g. NCX 4050 showed vasorelaxing activity on the aortas.

L9 ANSWER 12 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 136:178015 MARPAT
TITLE: Drugs for incontinence - salified and nonsalified nitric oxide-donors and phosphodiesterase inhibitors
INVENTOR(S): Del Soldato, Piero; Benedini, Francesca
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011707	A2	20020214	WO 2001-EP8734	20010727
WO 2002011707	A3	20021205		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM,				

DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IT 1318674	B1	20030827	IT 2000-MI1848	20000808
AU 2001091691	A5	20020218	AU 2001-91691	20010727
EP 1307184	A2	20030507	EP 2001-971798	20010727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511436	T2	20040415	JP 2002-517044	20010727
US 2003203899	A1	20031030	US 2003-343330	20030206
PRIORITY APPLN. INFO.:			IT 2000-MI1848	20000808
			WO 2001-EP8734	20010727

AB Use in the incontinence of one or more of the following classes of drugs selected from the following: (B) salified and nonsalified nitric oxide-donor drugs, of formula: A - X1 - N(O)z, (B') nitrate salts of drugs used for the incontinence, and which do not contain in the mol. a nitric oxide donor group; (C) organic or inorg. salts of compds. inhibiting phosphodiesterases.

L9 ANSWER 13 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:231708 MARPAT
TITLE: New self emulsifying drug delivery system
INVENTOR(S): Holmberg, Christina; Siekmann, Britta
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066088	A1	20010913	WO 2001-SE467	20010306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2401498	AA	20010913	CA 2001-2401498	20010306
EP 1267832	A1	20030102	EP 2001-910305	20010306
EP 1267832	B1	20040602		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001009014	A	20030603	BR 2001-9014	20010306
JP 2003525894	T2	20030902	JP 2001-564741	20010306
EE 200200500	A	20040216	EE 2002-500	20010306
AT 268162	E	20040615	AT 2001-910305	20010306
NZ 521009	A	20040625	NZ 2001-521009	20010306

PT 1267832	T	20040930	PT 2001-910305	20010306
ES 2220728	T3	20041216	ES 2001-1910305	20010306
ZA 2002006740	A	20031124	ZA 2002-6740	20020822
US 2003161846	A1	20030828	US 2002-220791	20020905
NO 2002004272	A	20021105	NO 2002-4272	20020906
PRIORITY APPLN. INFO.:			SE 2000-773	20000308
			WO 2001-SE467	20010306

AB The present invention claims and discloses a pharmaceutical composition suitable for oral administration, in form of an emulsion pre-concentrate, comprising: 1 or more NO-releasing NSAID(s), 1 or more surfactants, optionally an addnl. oil or semi-solid fat. The composition forms an in-situ oil-in-water emulsion upon contact with gastrointestinal fluids. The composition may optionally also comprise 1 or more short-chain alcs. Also within the scope of the invention is a combination with a proton pump inhibitor. The pharmaceutical composition is useful in the treatment of pain and inflammation. Further within the scope of the invention is kit comprising a pharmaceutical composition according to the invention in a unit dosage form, in combination with a proton pump inhibitor, and the proton pump inhibitor is enteric coated. Thus, a semisolid formulation contained a NO-releasing NSAID 750, Pluronic F127 450, and omeprazole 20 g.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:310142 MARPAT
TITLE: Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061537	A2	20001019	WO 2000-EP3234	20000411
WO 2000061537	A3	20010927		
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1311924	B1	20020320	IT 1999-MI753	19990413
CA 2370412	AA	20001019	CA 2000-2370412	20000411
BR 2000009702	A	20020108	BR 2000-9702	20000411
EP 1169294	A2	20020109	EP 2000-925203	20000411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541233	T2	20021203	JP 2000-610814	20000411
NZ 514267	A	20040625	NZ 2000-514267	20000411
RU 2237657	C2	20041010	RU 2001-127576	20000411

AU 778989	B2	20041223	AU 2000-44001	20000411
ZA 2001008127	A	20030103	ZA 2001-8127	20011003
NO 2001004927	A	20011213	NO 2001-4927	20011010
US 6869974	B1	20050322	US 2001-926326	20011015
PRIORITY APPLN. INFO.:			IT 1999-MI753	19990413
			WO 2000-EP3234	20000411

AB Compds. A-B-C-N(O)s and A-C1[N(O)s]-B1 or their salts [s is an integer 1 or 2, preferably s = 2; A is the radical of a drug and is such as to meet the pharmacol. tests reported in the description; C and C1 are two bivalent radicals; the precursors of the radicals B and B1 are such as to meet the pharmacol. test reported in the description] were prepared for use as pharmaceuticals. Thus, (S,S)-N-acetyl-S-(6-methoxy-α-methyl-2-naphthalenylacetyl)cysteine 4-nitroxybutyl ester was prepared (NCX 2101) from naproxene and N-acetylcysteine in the first of 28 synthetic examples given. Pharmacol. test examples and tabular data are also given.

L9 ANSWER 15 OF 19 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	133:152268 MARPAT
TITLE:	Synthesis method of (nitroxymethyl)phenyl esters of aspirin derivatives
INVENTOR(S):	Del Soldato, Piero; Garufi, Michele
PATENT ASSIGNEE(S):	Nicox S.A., Fr.
SOURCE:	PCT Int. Appl., 22 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044705	A1	20000803	WO 2000-EP353	20000118
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1307928	B1	20011129	IT 1999-MI134	19990126
CA 2361454	AA	20000803	CA 2000-2361454	20000118
BR 2000007643	A	20011016	BR 2000-7643	20000118
EP 1147074	A1	20011024	EP 2000-904925	20000118
EP 1147074	B1	20050323		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002535380	T2	20021022	JP 2000-595962	20000118
AU 766497	B2	20031016	AU 2000-26645	20000118
RU 2232747	C2	20040720	RU 2001-120697	20000118
ZA 2001005705	A	20021011	ZA 2001-5705	20010711
US 6512137	B1	20030128	US 2001-868932	20010717
PRIORITY APPLN. INFO.:			IT 1999-MI134	19990126
			WO 2000-EP353	20000118

AB RCO2H [R = substituted Ph, substituted (phenylcarbonyloxy)phenyl, etc.] were manufactured by (A) esterification of acyl halides RCOX (X = Cl, Br; R as above) with an isomer of hydroxybenzaldehyde in the presence of a base, (B) reduction of aldehyde group of the intermediate ester to give a (hydroxymethyl)phenyl ester, (C) halogenation of the latter

ester, e.g., with SOCl2 to obtain the corresponding (chloromethyl)phenyl ester, and (D) reaction of the chlorinated product with an inorg. nitrate salt, e.g., AgNO3. For example, 2-AcOC6H4CO2C6H4(CH2ONO2)-3 was prepared as described above.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 129:67686 MARPAT
TITLE: Preparation of arylalkylcarboxylate esters derived from nitrated cycloaliphatic alcohols which are useful as analgesic, antiinflammatory and antithrombotic agents
INVENTOR(S): Droux, Serge; Gigliotti, Giuseppe; Joly, Pascal; Petit, Francis
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Fr.; Droux, Serge; Gigliotti, Giuseppe; Joly, Pascal; Petit, Francis
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9825918	A1	19980618	WO 1997-FR2255	19971210
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2757159	A1	19980619	FR 1996-15272	19961212
FR 2757159	B1	19991217		
PRIORITY APPLN. INFO.:			FR 1996-15272	19961212

AB The invention concerns products Ar-(CHR1)p-C(O)O-(CH2)n-A-(CH2)m-ONO2 (I, Ar = aromatic monocyclic or bicyclic radical comprising 5-10 C atoms and optionally 1 or 2 heteroatoms selected from N, O or S, said radical being itself substituted or not; R1 = H, Me, or Et, n = 0-8, m = 0-8, n + m = 0-8, p = 0 or 1, A = bivalent radical derived from a saturated cyclic hydrocarbon containing 3-8 C atoms, optionally substituted, being understood that when m = 0 the saturated cyclic hydrocarbon does not contain 5-7 C atoms and that A is not linked to the groups Ar-(CHR1)p-C(O)O-(CH2)n and (CH2)m-ONO2 by the same C atom). The invention also concerns the method for preparing I and the intermediate products of this method. The claimed methods comprise esterification of Ar-(CHR1)p-C(O)OH with HO-(CH2)n-A-(CH2)m-ONO2 or esterification with HO-(CH2)n-A-(CH2)m-Z (Z = halo, OH) to give Ar-(CHR1)p-C(O)O-(CH2)n-A-(CH2)m-Z, followed by nitration. Intermediates used in the latter method are also claimed. Application of I as drugs and the pharmaceutical compns. containing them are claimed. Compds. I are useful as analgesic, antiinflammatory and antithrombotic agents.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:217188 MARPAT
TITLE: Preparation of nitric ester derivatives and their use in urinary incontinence and other diseases

INVENTOR(S): Del Soldato, Piero; Sannicolo', Francesco
PATENT ASSIGNEE(S): Nicox S.A., Fr.; Del Soldato, Piero; Sannicolo', Francesco
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809948	A2	19980312	WO 1997-EP4774	19970902
WO 9809948	A3	19980604		
W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2264081	AA	19980312	CA 1997-2264081	19970902
AU 9743010	A1	19980326	AU 1997-43010	19970902
AU 729533	B2	20010201		
EP 931065	A2	19990728	EP 1997-919021	19970902
EP 931065	B1	20040728		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, FI, RO				
BR 9712008	A	19990824	BR 1997-12008	19970902
CN 1234792	A	19991110	CN 1997-199130	19970902
JP 2000517332	T2	20001226	JP 1998-512226	19970902
RU 2210563	C2	20030820	RU 1999-106676	19970902
EP 1437132	A1	20040714	EP 2004-101544	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
AT 271858	E	20040815	AT 1997-919021	19970902
EP 1473288	A1	20041103	EP 2004-102724	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, FI, RO				
ES 2224237	T3	20050301	ES 1997-919021	19970902
AU 764127	B2	20030814	AU 2001-38954	20010427
US 2004082652	A1	20040429	US 2003-686907	20031017
PRIORITY APPLN. INFO.:			IT 1996-MI1821	19960904
			AU 1997-43010	19970902
			EP 1997-919021	19970902
			WO 1997-EP4774	19970902
			US 1999-147770	19990428

AB R(COX)tX1NO2 [I; R = e.g., residue of non-steroidal antiinflammatory agent; X = O or (alkyl)imino; X1 = e.g., ZCH2O; Z = 1,3-phenylene], displaying cyclooxygenase inhibiting and myorelaxing effect related to opening of Ca channels and/or release of NO in lower urinary tract, were prepared Thus, flufenamic acid was esterified by 3-(HO)C6H4CH2ONO2 to give 3-(F3C)C6H4NHZ1CO2C6H4(CH2ONO2)-3 (Z1 = 1,2-phenylene). Data for biol. activity of I were given.

L9 ANSWER 18 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 124:201789 MARPAT
TITLE: Preparation of aryl nitrate ester compounds having antiinflammatory ans well as analgesic and antithrombotic activities

INVENTOR(S): Del Soldato, Piero; Sannicolo', Francesco
PATENT ASSIGNEE(S): Nicox Ltd., Ire.
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9530641	A1	19951116	WO 1995-EP1233	19950404
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2190087	AA	19951116	CA 1995-2190087	19950404
AU 9522156	A1	19951129	AU 1995-22156	19950404
AU 702662	B2	19990225		
EP 759899	A1	19970305	EP 1995-915185	19950404
EP 759899	B1	19990915		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
HU 75961	A2	19970528	HU 1996-3107	19950404
BR 9507634	A	19970923	BR 1995-7634	19950404
JP 09512798	T2	19971222	JP 1995-528615	19950404
AT 184589	E	19991015	AT 1995-915185	19950404
ES 2139199	T3	20000201	ES 1995-915185	19950404
RU 2145595	C1	20000220	RU 1996-123280	19950404
US 5861426	A	19990119	US 1997-737426	19970306
US 5780495	A	19980714	US 1997-902570	19970729
GR 3032078	T3	20000331	GR 1999-403169	19991208

PRIORITY APPLN. INFO.: IT 1994-MI916 19940510
IT 1994-MI1731 19940809
GB 1993-20599 19931006
WO 1995-EP1233 19950404
US 1996-624508 19960405

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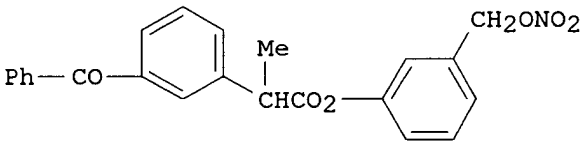


I

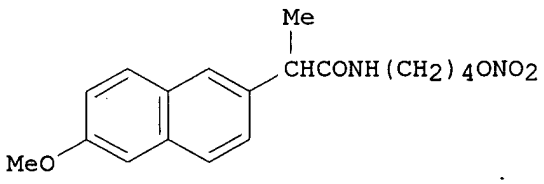
AB The title compds. AX1NO2 [A = R(COXu)t; t = 0, 1; u = 0, 1; X = O, (un)substituted NH or NR1c wherein R1c = alkyl; R = (un)substituted Ph, etc.; X = YO; Y = alkylene, cycloalkylene, oxyalkyl, etc.] (e.g., I), which inhibit cyclooxygenase, are prepared

L9 ANSWER 19 OF 19 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 123:82961 MARPAT
TITLE: Preparation of organic nitrate esters having antiinflammatory and/or analgesic activity
INVENTOR(S): Del Soldato, Piero

PATENT ASSIGNEE(S): Nicox Ltd., Ire.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9509831	A1	19950413	WO 1994-EP3182	19940923
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
GB 2283238	A1	19950503	GB 1993-20599	19931006
GB 2283238	B2	19971126		
CA 2173582	AA	19950413	CA 1994-2173582	19940923
AU 9478092	A1	19950501	AU 1994-78092	19940923
AU 678063	B2	19970515		
EP 722434	A1	19960724	EP 1994-928801	19940923
EP 722434	B1	19980729		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
HU 74446	A2	19961230	HU 1996-874	19940923
HU 218923	B	20001228		
BR 9407749	A	19970212	BR 1994-7749	19940923
JP 09503214	T2	19970331	JP 1994-510585	19940923
AT 168986	E	19980815	AT 1994-928801	19940923
ES 2120070	T3	19981016	ES 1994-928801	19940923
RU 2136653	C1	19990910	RU 1996-108907	19940923
US 5700947	A	19971223	US 1996-624508	19960405
US 5780495	A	19980714	US 1997-902570	19970729
PRIORITY APPLN. INFO.:			GB 1993-20599	19931006
			IT 1994-MI916	19940510
			WO 1994-EP3182	19940923
			US 1996-624508	19960405

OTHER SOURCE(S): CASREACT 123:82961
GI



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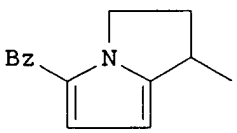

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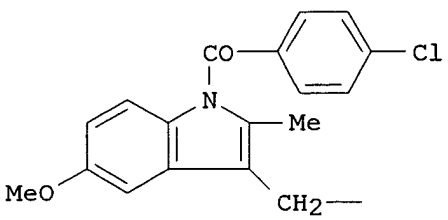
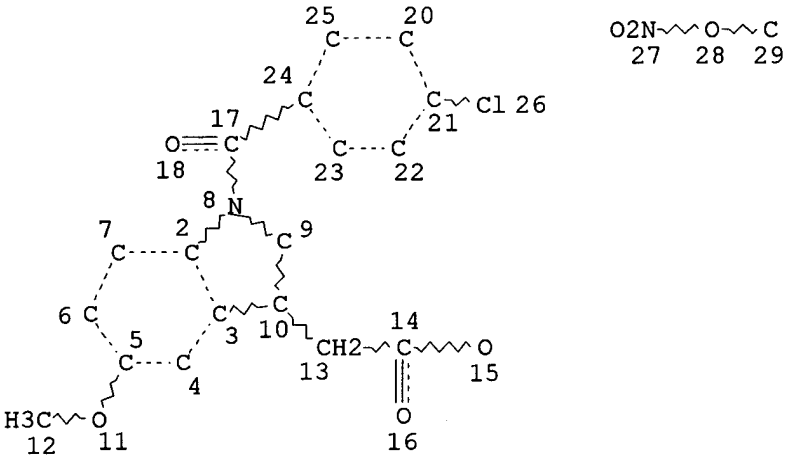


AB The title compds. MCOY[C(A)(B)]nONO2 [A, B = H, (un)branched alkyl; M = Q1, Q2, 2-(6-methoxy)naphthyl, etc.; n = 1-10], useful as analgesics, antiinflammatory agents, and blood platelet aggregation inhibitors, are prepared Thus, 2-(6-methoxy-2-naphthyl)propionic acid was converted into its Na carboxylate salt with NaOEt, the salt condensed with 1-bromo-4-chlorobutane, and the 4-chlorobutyl 2-(6-methoxy-2-naphthyl)propionate intermediate nitrated by reaction with AgNO3, producing the 4-nitratobutyl ester, II.

FILE 'MARPATPREV' ENTERED AT 11:13:03 ON 22 APR 2005

L1 STR



NODE ATTRIBUTES:
NSPEC IS RC AT 29
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L10 0 SEA FILE=MARPATPREV SSS FUL L1 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:13:36 ON 22 APR 2005)

L11 892 S "DEL SOLDATO P"?/AU
L12 216 S "SANNICOLO F"?/AU Author(s)
L13 16 S L11 AND L12
L14 14 S (L11 OR L12) AND (BLADDER OR INCONTINENC?)
L15 28 S L13 OR L14
L16 15 DUP REM L15 (13 DUPLICATES REMOVED)

Searcher : Shears 571-272-2528

L16 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:122770 CAPLUS
DOCUMENT NUMBER: 136:178015
TITLE: Drugs for **incontinence** - salified and nonsalified nitric oxide-donors and phosphodiesterase inhibitors
INVENTOR(S): **Del Soldato, Piero**; Benedini, Francesca
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011707	A2	20020214	WO 2001-EP8734	20010727
WO 2002011707	A3	20021205		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 1318674	B1	20030827	IT 2000-MI1848	20000808
AU 2001091691	A5	20020218	AU 2001-91691	20010727
EP 1307184	A2	20030507	EP 2001-971798	20010727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511436	T2	20040415	JP 2002-517044	20010727
US 2003203899	A1	20031030	US 2003-343330	20030206

PRIORITY APPLN. INFO.: IT 2000-MI1848 A 20000808
WO 2001-EP8734 W 20010727

OTHER SOURCE(S): MARPAT 136:178015
AB Use in the **incontinence** of one or more of the following classes of drugs selected from the following: (B) salified and nonsalified nitric oxide-donor drugs, of formula: A - X1 - N(O)z, (B') nitrate salts of drugs used for the **incontinence**, and which do not contain in the mol. a nitric oxide donor group; (C) organic or inorg. salts of compds. inhibiting phosphodiesterases.

L16 ANSWER 2 OF 15 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:283010 BIOSIS
DOCUMENT NUMBER: PREV200200283010
TITLE: Process for the preparation of a pharmacologically active chemical combination.
AUTHOR(S): **Sannicolo' , Francesco** [Inventor, Reprint author]; Benincori, Tiziana [Inventor]; **Del Soldato, Piero** [Inventor]
CORPORATE SOURCE: Milan, Italy
ASSIGNEE: Laboratori Alchemica S.r.l., Milan, Italy; Nicox SA, Valbonne-Sophia Antipolis, France

Searcher : Shears 571-272-2528

PATENT INFORMATION: US 6369260 April 09, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 9, 2002) Vol. 1257, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 8 May 2002
Last Updated on STN: 8 May 2002

AB Process for the preparation of a pharmacologically active chemical combination constituted by the association, through chemical bonds, of units equal to one another, having each an own pharmacological activity, and with the general formula (I): M--A--X--B--M, where M indicates said unit having an own pharmacological activity, X indicates a "bidentate" structure suitable to interconnect the M units, A and B indicate functional groups either equal to or different from one another which allow the interconnection between M and X.

L16 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:196587 CAPLUS
DOCUMENT NUMBER: 137:27642
TITLE: Nitric-oxide releasing molecules: a new class of drugs with several major indications
AUTHOR(S): Burgaud, J. L.; Riffaud, J. P.; **Del Soldato, P.**
CORPORATE SOURCE: NicOx, Gaia II, Sophia-Antipolis, 06906, Fr.
SOURCE: Current Pharmaceutical Design (2002), 8(3), 201-213
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Nitric oxide (NO) deficiency has been implicated in many pathol. and physiol. processes within the mammalian body providing a plausible biol. basis for the use of NO replacement therapy in these conditions. Exogenous NO sources may hopefully constitute a powerful way to supplement NO when the body cannot generate enough for normal biol. functions. This theory has opened up the possibility of designing new drugs that are capable of delivering NO into tissues and the bloodstream in a sustained and controlled manner. This objective has been reached by grafting an organic nitrate structure onto existing mols. with various spacers such as aliphatic or aromatic chain, with different degree of complexity. This approach has led to the synthesis of several new chemical entities in various pharmacol. classes, whose profile seems to challenge the parent drug not only on the basis of new pharmacol. properties but also on a better toxicol. and safety profile. In this article, general aspects on NO and NO donors are reviewed. Major focus is placed upon recent developments of novel NO donors, NO releasing device(s) as well as innovative improvements to conventional NO donors. Several examples are given in some important therapeutic indications such as cardiovascular diseases (NO-aspirin), pain and inflammation (NO-paracetamol), osteoporosis and urinary **incontinence** (NO flurbiprofen with aliphatic spacer), Alzheimer's disease (NO-flurbiprofen with anti-oxidant spacer), respiratory disorders (NO-steroids).

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-234905 [24] WPIDS
DOC. NO. CPI: C2001-070327
TITLE: New compounds including drug groups used for treating oxidative stress and/or endothelial disorders of moderate intensity.
DERWENT CLASS: B05
INVENTOR(S): **DEL SOLDATO, P**; DEL SOLDATA, P
PATENT ASSIGNEE(S): (NICO-N) NICOX SA
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001012584	A2	20010222	(200124)*	EN	93
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AU BA BB BG BR CA CN CR CU CZ DM EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ PL RO SG SI SK TR TT UA US UZ VN YU ZA					
AU 2000065670	A	20010313	(200134)		
BR 2000013264	A	20020416	(200234)		
NO 2002000623	A	20020409	(200238)		
KR 2002032552	A	20020503	(200270)		
EP 1252133	A2	20021030	(200279)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
IT 1314184	B	20021206	(200317)		
JP 2003515526	W	20030507	(200331)		116
HU 2002003939	A2	20030328	(200333)		
ZA 2002000628	A	20030625	(200348)		110
CN 1433396	A	20030730	(200365)		
MX 2002001519	A1	20030701	(200366)		
NZ 516889	A	20041029	(200474)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001012584	A2	WO 2000-EP7225	20000727
AU 2000065670	A	AU 2000-65670	20000727
BR 2000013264	A	BR 2000-13264	20000727
		WO 2000-EP7225	20000727
NO 2002000623	A	WO 2000-EP7225	20000727
		NO 2002-623	20020208
KR 2002032552	A	KR 2002-701883	20020209
EP 1252133	A2	EP 2000-953102	20000727
		WO 2000-EP7225	20000727
IT 1314184	B	IT 1999-MI1817	19990812
JP 2003515526	W	WO 2000-EP7225	20000727
		JP 2001-516885	20000727
HU 2002003939	A2	WO 2000-EP7225	20000727
		HU 2002-3939	20000727
ZA 2002000628	A	ZA 2002-628	20020123
CN 1433396	A	CN 2000-814049	20000727
MX 2002001519	A1	WO 2000-EP7225	20000727
		MX 2002-1519	20020211
NZ 516889	A	NZ 2000-516889	20000727
		WO 2000-EP7225	20000727

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000065670	A	Based on	WO 2001012584
BR 2000013264	A	Based on	WO 2001012584
EP 1252133	A2	Based on	WO 2001012584
JP 2003515526	W	Based on	WO 2001012584
HU 2002003939	A2	Based on	WO 2001012584
MX 2002001519	A1	Based on	WO 2001012584
NZ 516889	A	Div in	NZ 535559
		Based on	WO 2001012584

PRIORITY APPLN. INFO: IT 1999-MI1817 19990812
AN 2001-234905 [24] WPIDS
AB WO 200112584 A UPAB: 20030113
NOVELTY - New compounds (I) including drug groups are new.
DETAILED DESCRIPTION - Compounds of formula A-B-N(O)s (I) are new.
s = 1 or 2, preferably 2;
A = R-T1;
R = a drug group;
T1 = (CO)t or (X)t;
X = O, S or NR1c;
t, t' = 0 or 1;
provided that when t = 1 when t' = 0 and t = 0 when t' = 1;
B = TB-X2-O;
TB = CO when t = 0 or X when t' = 0;
X2 = a bivalent group such that the corresponding precursor TB-X2-OH of B does not meet test 5 and meets test 4A and TB = CO and t = 0, with the free valence of TB saturated with OZ or ZI-N(ZII) or TB = X and t' = 0 and the free valence of TB is saturated with H;
Z = H or R1a;
R1a = 1-10 (preferably 1-5)C alkyl and
ZI, ZII = a group Z;
provided that the drug A = R-T1, where the free valence is saturated when t' = 0, with OZ or ZI-N(ZII) and when t = 0 with X-Z meets at least one of tests 1-3.
Test 1 (NEM) is a test carried out in vivo on 4 groups of rats (each group containing 10 rats), the controls (2 groups) and the treated (2 groups) of which one group of the controls and one group of the treated respectively are administered with one dose of 25 mg/kg subcutaneously N-ethylmaleimide (NEM). The controls are treated with the carrier and the treated groups with carrier and drug A = R-T1 with saturated free valence. The drug is administered at a dose equivalent to the maximum dose tolerated by the rats that did not receive NEM. The drug can be used to prepare (I) when the group treated with NEM, carrier and drug shows gastrointestinal damage or in the group treated with NEM, carrier and drug are observed gastrointestinal damage greater than that of the group treated with carrier or of the group treated with the carrier and NEM.
Test 2 (CIP) is an in vitro test where human endothelial cells from the umbilical vein are harvested under standard conditions, then divided into 2 groups (each replicated 5 times), of which one is treated with a mixture of the drug 10-4 concentration in culture medium and the other group with carrier. Then cumene hydroperoxide (CIP) having 5 mM concentration in the culture medium is added to each group. The drug can be use to prepare (I) when a statistically

significant inhibition of the apoptosis induced by CIP is not obtained with p less than 0.01 with respect to the group treated with carrier and CIP.

Test 3 (l-NAME) is an in vivo test carried out on 4 groups of rats (each containing 10 rats) for 4 weeks and receiving drinking water, the controls (2 groups) and the treated (2 groups), of which 1 group of controls and of treated respectively receive in the above weeks water containing N- omega -nitro-L-arginine methyl ester (L-NAME) at a concentration of 400 mg/l. Controls in the 4 weeks are administered with carrier and the treated in the 4 weeks with carrier and drug, each once a day. The drug is administered at the maximum dose tolerated by the group of rats not pretreated with L-NAME. After 4 weeks, water supply is stopped for 24 hours and then the rats are sacrificed. Blood pressure is determined 1 hour before sacrifice. After sacrifice, the plasma glutamic pyruvic transaminase (GPT) is determined and the gastric tissue is examined. The drug can be used to prepare (I) when in group treated with L-NAME, carrier and drug, greater hepatic damage and/or cardiovascular damage are found in comparison respectively with the group treated with the carrier or carrier and drug or carrier and L-NAME.

Test 4A met by the compound precursor B is an in vitro test in which part of an erythrocyte suspension kept at 4 deg. C for 4 days and isolated from Wistar male rats and suspended in physiological solution buffered at pH 7.4 with phosphate buffer, is centrifuged at 1000 rpm for 5 minutes. 0.1 ml Centrifuged erythrocytes are diluted with sodium phosphate buffer pH 7.4 at 50 ml. Aliquots of 3.5 ml are taken and incubated at 37degC in the presence of cumene hydroperoxide at a concentration of 270 mu M and the suspension turbidity determined at 710 nm at intervals of 30 minutes to establish the time (Tmax) at which occurs the maximum turbidity that corresponds to the maximum amounts of cells lysed by cumene hydroperoxide (haemolysis assumed to be 100%). Alcoholic solutions of the compounds precursors of B are added to 3.5 ml aliquots of the dilutes suspension of centrifuged erythrocytes to give a final concentration of 2 mm of the precursor of B. Resulting suspension is preincubated for 30 minutes. Cumene hydroperoxide is added to give the same above indicated final concentration and at Tmax is determined the percentage of haemolysis inhibition in the sample from the ratio, multiplied by 100, between absorbance of sample containing erythrocytes, precursor of B and cumene hydroperoxide respectively and that of sample containing erythrocytes and cumene hydroperoxide. Precursors of B meet the test if they inhibit haemolysis induced by cumene hydroperoxide by more than 15%.

Test 5 is an analytical determination carried out by adding aliquots of 10-4 M methanol solutions of precursor B or B1 or of C = Tc-Y-H, having the free valence saturated, to solution formed by admixing 2 mM solution of deoxyribose in water with 100 mM phosphate buffer and 1 mu M FeII(NH4)2(SO4)2. After thermostating at 37 deg. C for 1 hour, aliquots of aqueous solutions of trichloroacetic acid (2.8%) and of thiobarbituric acid (0.5M) are added and heating is effected at 100 deg. C for 15 minutes. Absorbance of tested solutions is read at 532 nm. Inhibition induced by precursor B or B1 or C = Tc-Y-H in the confront of radical production by FeII is calculated as a percentage by using (1-As/Ac) x 100.

As and Ac are respectively absorbance values of solution containing tested compound and iron salt and that of solution containing iron salt. Test 5 is met when inhibition percentage is at least 50%.

In (I), when X2 of B is 1-20C alkylene or 5-7C cycloalkylene

(optionally substituted), the drugs of formula A = R-T1 with free valence saturated, do not belong to drugs used in **incontinence**, antithrombotic drugs (ACE inhibitors), prostaglandins and anti-inflammatory drugs (NSAIDs and corticosteroids), but not excluding paracetamol and sulindac.

N.B. The definitions given in the specification are not clear.

ACTIVITY - Antioxidant; cardiant; vasotropic; hypotensive; cerebroprotective; antiarteriosclerotic; antiarthritic; anti-inflammatory; neuroprotective; dermatological; antibacterial.

MECHANISM OF ACTION - None given.

USE - Used for treating oxidative stress and/or endothelial dysfunctions of moderate intensity, which cause myocardial and vascular ischemia, hypertension, stroke, arteriosclerosis, rheumatoid arthritis and connected inflammatory diseases, asthma and connected inflammatory diseases, ulcerative and non ulcerative dyspepsias, intestinal inflammatory diseases, Alzheimer's disease, impotence, **incontinence**, eczema, neurodermatitis, acne and infectious diseases.

ADVANTAGE - (I) Have higher efficacy and lower toxicity.

Dwg.0/0

L16 ANSWER 5 OF 15 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:426837 BIOSIS
DOCUMENT NUMBER: PREV200000426837
TITLE: Compounds and their compositions having anti-inflammatory and anti-thrombotic activities.
AUTHOR(S): **Del Soldato, Piero** [Inventor, Reprint author]; **Sannicolo' , Francesco** [Inventor]
CORPORATE SOURCE: Milan, Italy
ASSIGNEE: Nicox S.A., Paris, France
PATENT INFORMATION: US 6040341 March 21, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar. 21, 2000) Vol. 1232, No. 3. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Oct 2000
Last Updated on STN: 10 Jan 2002

AB Compounds and their compositions, of general formula: A--X1 --NO2 are used as medicaments wherein: A=R(COX)t t=0 or 1; X=O and the remaining substituents are defined in the specification.

L16 ANSWER 6 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2000-679460 [66] WPIDS
DOC. NO. CPI: C2000-206609
TITLE: New steroidal compounds for treating conditions associated with oxidative stress and endothelial dysfunction have improved tolerability.
DERWENT CLASS: B01
INVENTOR(S): **DEL SOLDATO, P**
PATENT ASSIGNEE(S): (NICO-N) NICOX SA
COUNTRY COUNT: 80
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000061604	A2	20001019	(200066)*	EN	102

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AL AU BA BB BG BR CA CN CU CZ DM EE GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US UZ VN YU ZA

AU	2000038201	A	20001114	(200108)	
EP	1169337	A2	20020109	(200205) EN	
	R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI				
BR	2000009696	A	20020108	(200208)	
NO	2001004925	A	20011213	(200211)	
KR	2001108489	A	20011207	(200236)	
IT	1311922	B	20020320	(200252)	
HU	2002001872	A2	20021028	(200277)	
JP	2002542162	W	20021210	(200301)	99
ZA	2001008124	A	20030326	(200327)	120
CN	1420891	A	20030528	(200357)	
MX	2001010212	A1	20020901	(200370)	
AU	766798	B	20031023	(200381)	
NZ	514572	A	20040326	(200425)	
AU	2004200263	A1	20040219	(200445)	
EP	1169337	B1	20040825	(200456) EN	
	R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU MC NL PT RO SE SI				
DE	60013266	E	20040930	(200465)	
EP	1475386	A2	20041110	(200473) EN	
	R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU MC NL PT SE				
RU	2240325	C2	20041120	(200504)	
ES	2226805	T3	20050401	(200524)	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000061604	A2	WO 2000-EP3238	20000411
AU 2000038201	A	AU 2000-38201	20000411
EP 1169337	A2	EP 2000-917075	20000411
		WO 2000-EP3238	20000411
BR 2000009696	A	BR 2000-9696	20000411
		WO 2000-EP3238	20000411
NO 2001004925	A	WO 2000-EP3238	20000411
		NO 2001-4925	20011010
KR 2001108489	A	KR 2001-712940	20011010
IT 1311922	B	IT 1999-MI751	19990413
HU 2002001872	A2	WO 2000-EP3238	20000411
		HU 2002-1872	20000411
JP 2002542162	W	JP 2000-611546	20000411
		WO 2000-EP3238	20000411
ZA 2001008124	A	ZA 2001-8124	20011003
CN 1420891	A	CN 2000-808774	20000411
MX 2001010212	A1	WO 2000-EP3238	20000411
		MX 2001-10212	20011009
AU 766798	B	AU 2000-38201	20000411
NZ 514572	A	NZ 2000-514572	20000411
		WO 2000-EP3238	20000411
AU 2004200263	A1	AU 2004-200263	20040122
EP 1169337	B1	EP 2000-917075	20000411
		WO 2000-EP3238	20000411
	Related to	EP 2004-102751	20000411

Searcher : Shears 571-272-2528

DE 60013266	E	DE 2000-00013266	20000411
		EP 2000-917075	20000411
		WO 2000-EP3238	20000411
EP 1475386	A2 Div ex	EP 2000-917075	20000411
		EP 2004-102751	20000411
RU 2240325	C2	WO 2000-EP3238	20000411
		RU 2001-127575	20000411
ES 2226805	T3	EP 2000-917075	20000411

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000038201	A	Based on	WO 2000061604
EP 1169337	A2	Based on	WO 2000061604
BR 2000009696	A	Based on	WO 2000061604
HU 2002001872	A2	Based on	WO 2000061604
JP 2002542162	W	Based on	WO 2000061604
MX 2001010212	A1	Based on	WO 2000061604
AU 766798	B	Previous Publ.	AU 2000038201
		Based on	WO 2000061604
NZ 514572	A	Based on	WO 2000061604
AU 2004200263	A1	Div ex	AU 766798
EP 1169337	B1	Based on	WO 2000061604
DE 60013266	E	Based on	EP 1169337
		Based on	WO 2000061604
EP 1475386	A2	Div ex	EP 1169337
RU 2240325	C2	Based on	WO 2000061604
ES 2226805	T3	Based on	EP 1169337

PRIORITY APPLN. INFO: IT 1999-MI751 19990413
AN 2000-679460 [66] WPIDS
AB WO 200061604 A UPAB: 20001219
NOVELTY - Steroidal compounds (I) and (II) are new.
DETAILED DESCRIPTION - Steroidal compounds of formula (I) and (II) and their salts are new.
s = 1 or 2;
b = 0 or 1;
A = radical obtained from a compound of formula (A);
B = TbX2Tb1;
Tb, Tc = CO (when the reactive function in the precursor steroid is OH) or X (when the reactive function in the precursor steroid is COOH);
X = O, S, NR1c or absent;
R1c = H or 1-5C alkyl;
Tb1, Tc1 = (CO)tx or (X)ty;
tx, ty = 0 or 1;
X2 = divalent bridging group such that the corresponding B precursor meets test 4 or test 5 with free valences in Tb and Tb1 being saturated with OZ, Z or NZZ;
Q = TcY and the Q precursor when b = 0 is TcYH with the Tc free valence saturated with OZ, Z or NZZ and meets test 5;
Tc, Tb2 = CO (when tx = 0) or X (when ty = 0);
Y = (CRt3Rt4)n9Y3(CRt5Rt6)n8O, OR', (CH2)n3Ph(CH2)n31O, (CH(CH2ONO2)O)nf, (CH(Rf1)CH2O)nf or (CH2CH(Rf1)O)nf;
Ph = phenylene optionally substituted by COOH;
n8, n9, n3 = 0-3;
Rt3-Rt6 = H or 1-4C alkyl;
Y3 = saturated, unsaturated or aromatic 5 or 6 membered

nitrogenous heterocyclyl;
R' = 1-20C alkylene or 5-7C cycloalkylene (optionally with one or more C replaced by heteroatoms and optionally substituted by R1 (sic));
n31 = 1-3;
nf = 1-6; R1f = H or Me;
Q1 = Tc1Y1Tc2;
Y1 = as Y but with three free valences instead of two;
B1 = Tb2X2a;
X2a = monovalent radical such that the corresponding precursor TB2X2a meets test 4 or 5 and the Tb2 free valence is saturated with Z, OZ or NZZ;
Z = not defined;
V1, V4, V5, V10, V3a, V11a, V16a = H;
V2 = H, Cl or Br;
V3 = H, OCH2CH2Cl or OH;
V6 = H, Cl, F, Me or CHO;
V7 = H, Cl or OH;
V9 = H, Cl or F;
V11 = H, OH, Cl or Me;
V16 = Me or OH;
V17 = OH, Me, OCO(O)ua(CH2)vaMe, CCH or OCOfuran2-yl; or
V3+V3a, V11+V11a = O;
or V16+V16a = CH2; or
V2+V3 = a group of formula (i);
V1+V2, V3+V4, V4+V5, V5+V6, V5+V10 = bond; or
V16+V17 = a group of formula (ii)-(iv);
R, R1 = H or 1-4C alkyl;
R2 = (COL)t(L)t2 (X1)t1;
t, t1, t2, ua = 0 or 1;
va = 0-4;
L = (CR4R5)na(O)nb(CR4R5)n1a(CO)nb(O)nb2(CO)nb3(CR4R5)na2;
na, na1, na2 = 0-6; nb, nb1, nb2 = 0 or 1;
R4, R5 = H or 1-5C alkyl;
X1 = O, S, NR1c1 or bond;
R1c1 = 1-10C alkyl, OH, Me (sic), Cl, NEt2, SCH2F, SH or 1-methyl-piperazin-4-yl;
test 4 = an analytical determination for a B or B1 precursor at 10-4M having an inhibition of equal to or greater than 50% for a 2,2-diphenyl-1-picryl hydrazyl (DPPH) free radical in methanol at room temperature in the absence of light for 30 minutes measured using absorbance at wavelength of 517 nm and calculated using the formula (1-As/Ac)x100;
test 5 = an analytical determination for a B, B1 or TcYH precursor of an inhibition concentration of greater than or equal to 50% for Fe (II) radical production by adding aliquots of a 10-4M methanolic solution of the precursor to a solution of 2 mM desoxyribose, in water with 100 mM phosphate buffer and 1 mM Fe (II)(NH4)2(SO4)2 at 37 deg. C for 1 hour, then treatment with aqueous trichloroacetic acid (2.8%) and then thiobarbituric acid (0.5 M), heating for 15 minutes at 100 deg. C and measuring absorbance at 532 nm using the formula (1-As/Ac)x100; As, Ac respectively = the absorbance values of the solution containing the test compound and DPPH (in test 4) or iron salt (in test 5) and absorbance in absence of test compound;
provided that (i) tx = 0 when ty = 1 and tx = 1 when ty = 0 (sic); (ii) t2 = 0 when t1 = 1 and t2 = 1 when t = 0; (iii) t and t1 or t2 and t1 are not both 0 when A does not contain OH; and (iv) compounds (I) in which b = 0, Q = TcY in which the free valence of Y

is saturated and s = 1 or 2 are excluded.

ACTIVITY - Antiinflammatory; Immunosuppressive; Cardiant; Hypotensive; Cerebroprotective; Antiarteriosclerosis; Antiarthritic; Antirheumatic; Antiasthmatic; Antiulcer; Nootropic; Uropathic; Dermatological; Antiacne; Antibacterial; Virucide.

Hepatic damage, determined by GPT assay for 3-(4-((3 alpha ,5 beta ,7 beta)-3,7-dihydoxycolan-24-oiloxy)-3-methoxyphenyl)-2-propenoic acid 4-nitroxybutyl ester (sic) (Ia) at 100 mg/kg i.p. in rats (not treated with L-NAME) was 103% GPT variation compared to 100% for control and 130% for ursodesoxycholic acid at 100 mg/kg i.p. The corresponding values for rats treated with L-NAME were 123%, 230% and 276% respectively.

MECHANISM OF ACTION - Antioxidant.

USE - For treating conditions associated with oxidative stress and/or endothelial dysfunction using steroids with antiinflammatory, immunodepressive, angiostatic and gastroinestinal activity. Example of pathological conditions caused by oxidative stress and/or endothelial dysfunction are e.g. cardiovascular system disorders (such as myocardial and vascular ischemia, hypertension, stroke and arteriosclerosis), connective tissue disorders (such as rheumatoid arthritis), pulmonary system disorders (such as asthma), gastrointestinal system disorders (such as ulcerative and non-ulcerative dyspepsias and intestinal inflammatory diseases), central nervous system disorders (such as Alzheimer's disease), urogenital system disorders (such as impotence and incontinence), cutaneous system disorders (such as eczema and acne) and infective diseases such as viral infection.

ADVANTAGE - Compounds have improved tolerability and/or efficacy compared to precursor steroids e.g. side effects on the liver are reduced.

Dwg.0/0

L16 ANSWER 7 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2000-687027 [67] WPIDS
DOC. NO. CPI: C2000-208962
TITLE: Nitro or Nitroso derivatives are used in the treatment of oxidative stress and/or endothelial dysfunction, in the treatment of the cardiovascular system hypertension, arteriosclerosis, rheumatoid arthritis, and the gastrointestinal system.
DERWENT CLASS: B05
INVENTOR(S): **DEL SOLDATO, P**
PATENT ASSIGNEE(S): (NICO-N) NICOX SA
COUNTRY COUNT: 80
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000061541	A2	20001019	(200067)*	EN	138
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AL AU BA BB BG BR CA CN CU CZ DM EE GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US UZ VN YU ZA					
AU 2000045474	A	20001114	(200108)		
EP 1169298	A2	20020109	(200205)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 2000009703	A	20020108	(200208)		

NO 2001004928	A	20011213	(200211)	
KR 2002005668	A	20020117	(200250)	
IT 1311923	B	20020320	(200252)	
CN 1358178	A	20020710	(200278)	
HU 2002000714	A2	20021228	(200308)	
JP 2002541236	W	20021203	(200309)	118
ZA 2001008126	A	20030625	(200348)	156
MX 2001010213	A1	20020901	(200370)	
NZ 514270	A	20040227	(200418)	
RU 2237057	C2	20040927	(200468)	
AU 777579	B2	20041021	(200501)	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000061541	A2	WO 2000-EP3239	20000411
AU 2000045474	A	AU 2000-45474	20000411
EP 1169298	A2	EP 2000-926870	20000411
		WO 2000-EP3239	20000411
BR 2000009703	A	BR 2000-9703	20000411
		WO 2000-EP3239	20000411
NO 2001004928	A	WO 2000-EP3239	20000411
		NO 2001-4928	20011010
KR 2002005668	A	KR 2001-712914	20011009
IT 1311923	B	IT 1999-MI752	19990413
CN 1358178	A	CN 2000-808491	20000411
HU 2002000714	A2	WO 2000-EP3239	20000411
		HU 2002-714	20000411
JP 2002541236	W	JP 2000-610818	20000411
		WO 2000-EP3239	20000411
ZA 2001008126	A	ZA 2001-8126	20011003
MX 2001010213	A1	WO 2000-EP3239	20000411
		MX 2001-10213	20011009
NZ 514270	A	NZ 2000-514270	20000411
		WO 2000-EP3239	20000411
RU 2237057	C2	WO 2000-EP3239	20000411
		RU 2001-127574	20000411
AU 777579	B2	AU 2000-45474	20000411

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000045474	A	Based on	WO 2000061541
EP 1169298	A2	Based on	WO 2000061541
BR 2000009703	A	Based on	WO 2000061541
HU 2002000714	A2	Based on	WO 2000061541
JP 2002541236	W	Based on	WO 2000061541
MX 2001010213	A1	Based on	WO 2000061541
NZ 514270	A	Based on	WO 2000061541
RU 2237057	C2	Based on	WO 2000061541
AU 777579	B2	Previous Publ.	AU 2000045474
		Based on	WO 2000061541

PRIORITY APPLN. INFO: IT 1999-MI752 19990413
AN 2000-687027 [67] WPIDS
AB WO 200061541 A UPAB: 20011105
NOVELTY - Nitro or Nitroso derivatives (I) and (II) and their salts

are new.

DETAILED DESCRIPTION - Nitro or Nitroso derivatives of formula (I) and (II) and their salts are new.

s = 1-2;

bo = 0-1;

A' = R-T1-;

R = drug radical;

T1 = (CO)t or (X)t';

t, t' = 0-1;

X = O, S or NR1C;

R1C = H, 1-5C alkyl or a free valence;

B' = -TB-X2-TBI-

TB = (CO) when t = 0 or X when t' = 0;

TBI = (CO)tx or (X)txx;

tx, txx = 0-1;

X2 = bivalent bridging bond;

C' = -Tc-Y'-;

Tc = (CO) when tx = 0 or X when txx = 0;

Y' = a group of formula (a), R'O or 5-7C cycloalkylene optionally with one or more carbons replaced with heteroatoms and optionally substituted by R'';

n = 0-3;

m = 1-3;

RTIX = H or 1-4C alkyl;

Y3 = 5-6 membered (un)saturated or aromatic heterocyclic ring containing at least 1 N;

R' = 1-20C alkyl;

R'' = R' or a group of foumula (b) - (e), -(CH(R1f)CH2O)nf or -(CH2CH(R11)O)nf;

C1' = a group of formula (f);

TCI = CO when t = 0 or X when t' = 0;

TCII = CO or X;

Y'' = a group of foumula (g) - (m) or 2-6C alkyl;

n3 = 0-3;

n3' = 1-3;

nf' = 1-6; and

R1f = H or CH3.

ACTIVITY - Cardiant; vasotropic; hypotensive, vasodilator; hypotensive; antiarteriosclerotic; antirheumatic; antiarthritic; antiinflammatory; gastrointestinal; antiulcer; nootropic; neuroprotective; cytostatic; dermatological; virucide; respiratory; beta blocker.

MECHANISM OF ACTION - No method of action given.

USE - (I) and (II) are used in the treatment of oxidative stress and/or endothelial dysfunction, in the treatment of the cardiovascular system e.g. myocardial and vascular ischemia, hypertension, stroke, arteriosclerosis, connective tissue e.g. rheumatoid arthritis, and connected inflammatory diseases, the gastrointestinal system e.g. ulcerative and nonulcerative dyspepsias, intestinal inflammatory diseases, central nervous system disorders e.g. Alzheimer's disease, the urogenital system e.g. impotence or incontinence, the cutaneous system e.g. eczema, neurodermatitis, acne and infectious diseases. (I) and (II) can also be used as antiinflammatories, beta blockers, bronchodilators, bone resorption inhibitor, phosphodiesterase inhibitors, antiallergics, anti-angiotenisn drugs, antidiabetics, or anti tumoral drugs.

ADVANTAGE - (I) and (I) have an improved therapeutic index as compared to precursor drugs.

Dwg.0/0

Searcher : Shears 571-272-2528

L16 ANSWER 8 OF 15 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:97107 BIOSIS
DOCUMENT NUMBER: PREV199900097107
TITLE: Nitro compounds of the formula A-X-1-NO-2 and their compositions having anti-inflammatory, analgesic and anti-thrombotic activities.
AUTHOR(S): **Del, Soldato, P.** [Inventor]; **Sannicolo, F.** [Inventor]
CORPORATE SOURCE: Milan, Italy
ASSIGNEE: NICOX S.A.
PATENT INFORMATION: US 5861426 Jan. 19, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 19, 1999) Vol. 1218, No. 3, pp. 2230-2233. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Mar 1999
Last Updated on STN: 4 Mar 1999

L16 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1999:731703 CAPLUS
DOCUMENT NUMBER: 132:202450
TITLE: HCT-1026: Treatment of septic shock, treatment of urinary **incontinence**, treatment of osteoporosis, nitric oxide donor
AUTHOR(S): Burgaud, J. L.; Benedini, F.; Robinson, E. M.; **Del Soldato, P.**
CORPORATE SOURCE: NicOx, Valbonne, 06560, Fr.
SOURCE: Drugs of the Future (1999), 24(8), 858-861
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 21 refs., describing the synthesis, pharmacol. actions, toxicity, and clin. uses of HCT-1026.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1998:175910 CAPLUS
DOCUMENT NUMBER: 128:217188
TITLE: Preparation of nitric ester derivatives and their use in urinary **incontinence** and other diseases
INVENTOR(S): **Del Soldato, Piero; Sannicolo', Francesco**
PATENT ASSIGNEE(S): Nicox S.A., Fr.; Del Soldato, Piero; Sannicolo', Francesco
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809948	A2	19980312	WO 1997-EP4774	19970902
WO 9809948	A3	19980604		
W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2264081	AA	19980312	CA 1997-2264081	19970902
AU 9743010	A1	19980326	AU 1997-43010	19970902
AU 729533	B2	20010201		
EP 931065	A2	19990728	EP 1997-919021	19970902
EP 931065	B1	20040728		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, FI, RO				
BR 9712008	A	19990824	BR 1997-12008	19970902
CN 1234792	A	19991110	CN 1997-199130	19970902
JP 2000517332	T2	20001226	JP 1998-512226	19970902
RU 2210563	C2	20030820	RU 1999-106676	19970902
EP 1437132	A1	20040714	EP 2004-101544	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
AT 271858	E	20040815	AT 1997-919021	19970902
EP 1473288	A1	20041103	EP 2004-102724	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, FI, RO				
ES 2224237	T3	20050301	ES 1997-919021	19970902
AU 764127	B2	20030814	AU 2001-38954	20010427
US 2004082652	A1	20040429	US 2003-686907	20031017
PRIORITY APPLN. INFO.:			IT 1996-MI1821	A 19960904
			AU 1997-43010	A3 19970902
			EP 1997-919021	A3 19970902
			WO 1997-EP4774	W 19970902
			US 1999-147770	A3 19990428

OTHER SOURCE(S): MARPAT 128:217188

AB R(COX)tX1NO2 [I; R = e.g., residue of non-steroidal antiinflammatory agent; X = O or (alkyl)imino; X1 = e.g., ZCH2O; Z = 1,3-phenylene], displaying cyclooxygenase inhibiting and myorelaxing effect related to opening of Ca channels and/or release of NO in lower urinary tract, were prepared Thus, flufenamic acid was esterified by 3-(HO)C6H4CH2ONO2 to give 3-(F3C)C6H4NHZ1CO2C6H4(CH2ONO2)-3 (Z1 = 1,2-phenylene). Data for biol. activity of I were given.

L16 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 1997:397389 CAPLUS

DOCUMENT NUMBER: 127:17490

TITLE: New acyloxybenzoate nitrate esters and their compositions having anti-inflammatory and anti-thrombotic activities

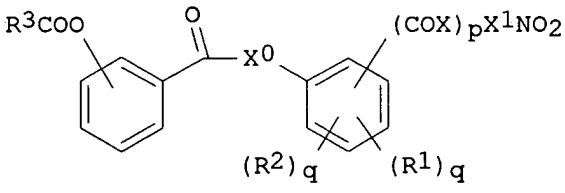
INVENTOR(S): **Del Soldato, Piero; Sannicolo', Francesco**

PATENT ASSIGNEE(S): Nicox S.A., Fr.; Del Soldato, Piero; Sannicolo',

Francesco
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9716405	A1	19970509	WO 1996-EP4696	19961029
W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2235996	AA	19970509	CA 1996-2235996	19961029
AU 9674950	A1	19970522	AU 1996-74950	19961029
AU 709338	B2	19990826		
EP 871606	A1	19981021	EP 1996-937282	19961029
EP 871606	B1	20000614		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, FI				
BR 9611175	A	19990330	BR 1996-11175	19961029
JP 11514636	T2	19991214	JP 1996-517060	19961029
AT 193883	E	20000615	AT 1996-937282	19961029
ES 2148808	T3	20001016	ES 1996-937282	19961029
PT 871606	T	20001130	PT 1996-937282	19961029
RU 2165921	C2	20010427	RU 1998-110565	19961029
US 6040341	A	20000321	US 1998-66344	19980429
GR 3033827	T3	20001031	GR 2000-401528	20000630
PRIORITY APPLN. INFO.:			IT 1995-MI2263 A	19951031
			WO 1996-EP4696 W	19961029

OTHER SOURCE(S): MARPAT 127:17490
GI



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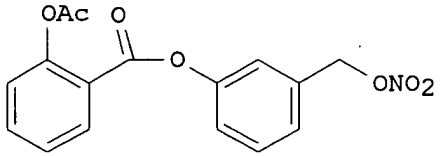

II

Searcher : Shears 571-272-2528

AB The title compds. and their compns. are disclosed, specifically the compds. I or their salts [wherein p, q = 0, 1; X = O, NH, alkylimino, [CH2CH(ONO2)CH2O]n, [CH2CH(R2a)O]n; R2a = H, Me; X0 = X; R1 = certain acyloxy; R2 = H, OH, halo, alkyl, alkoxy, perfluoroalkyl, NO2, (di)(alkyl)amino; or R1R2 = OCH2O; R3 = alkyl; X1 = bivalent linking group chosen from YO or [CH2CH(R2a)O]n(YO)m; Y = (un)substituted linear or branched C1-20 alkylene or C5-7 cycloalkylene; n = 1-6; m = 0 or 1]. The compds. are cyclooxygenase inhibitors, and have good antiinflammatory activity combined with low toxicity. For instance, 3-HOC6H4CH2OH reacted with 48% HBr to give 3-HOC6H4CH2Br, which reacted with AgNO3 in MeCN to give 3-HOC6H4CH2ONO2. The latter reacted with 2-AcOC6H4COCl and K2CO3 in EtOAc to give title compound II. At 10-4 M in vitro, II reduced piastrinic aggregation induced by arachidonic acid to 0% of control, vs. only 50% for the known agent 2-AcOC6H4CO2(CH2)4ONO2 (preparation given). No acute toxicity was observed for either compound in rats at an oral dose of 200 mg/kg.

L16 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1998:108659 CAPLUS
DOCUMENT NUMBER: 128:212528
TITLE: NCX-4016. Antiinflammatory analgesic antithrombotic
AUTHOR(S): Cirino, Giuseppe; Calignano, Antonio; **Sannicolo, Franco**; Prinavera, Angelo; **Del Soldato, Piero**; Wallace, John L.
CORPORATE SOURCE: Dept. of Experimental Pharmacology, University of Naples, via Domenico Montesano 49, Naples, 80131, Italy
SOURCE: Drugs of the Future (1997), 22(11), 1231-1233
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: J. R. Prous, S.A.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 18 refs.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1998:272236 CAPLUS
DOCUMENT NUMBER: 129:35946
TITLE: Gastrointestinal-sparing anti-inflammatory drugs: the development of nitric oxide-releasing NSAIDs
AUTHOR(S): Wallace, John L.; Elliott, Susan N.; **Del Soldato, Piero**; Mcknight, Webb; **Sannicolo, Franco**; Cirino, Giuseppe
CORPORATE SOURCE: Department of Pharmacology, The University of Calgary, Calgary, AB, T2N 4N1, Can.
SOURCE: Drug Development Research (1997), 42(3/4), 144-149
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 36 refs., nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most widely prescribed medications, but their use continues to be limited by significant toxicity, particularly in the gastrointestinal tract and kidney. Better understanding of the pathogenesis of these adverse effects has led to the development of a series of derivs. of standard NSAIDs that are not only less toxic but more

efficacious. The coupling of a nitric oxide-releasing moiety to a range of NSAIDs greatly reduces their ability to induce gastrointestinal damage, and greatly increases their tolerability in situations in which there is preexisting gastrointestinal inflammation. There is also evidence that these compds. are much better tolerated by the kidney. On the other hand, the analgesic and anti-thrombotic properties of NO-releasing NSAIDs significantly exceed those of the parent drugs. These compds. appear to represent a significant advance in the treatment of inflammation and pain and for prophylaxis of thrombotic conditions.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1996:473193 CAPLUS
DOCUMENT NUMBER: 125:114476
TITLE: Preparation of diol bis-(benzoates or heterocyclylcarboxylates) as antiinflammatory agents and platelet aggregation inhibitors
INVENTOR(S): **Del Soldato, Piero; Sannicolo, Francesco;** Benincori, Tiziana
PATENT ASSIGNEE(S): Laboratori Alchemia S.R.L., Italy
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9615809	A2	19960530	WO 1995-EP4556	19951120
WO 9615809	A3	19961017		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9641741	A1	19960617	AU 1996-41741	19951120
EP 793507	A2	19970910	EP 1995-940211	19951120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
EP 1038534	A2	20000927	EP 2000-105715	19951120
EP 1038534	A3	20010404		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 6369260	B1	20020409	US 1997-836756	19970516

PRIORITY APPLN. INFO.:		
IT 1994-MI2362	A	19941122
EP 1995-940211	A3	19951120
WO 1995-EP4556	W	19951120

OTHER SOURCE(S): MARPAT 125:114476
AB The title compds. M-A-X-B-M [I; M = 2-AcOC6H4CO; 3-(PhCO)C6H4CH(Me)CO; etc.; A, B = O, S, NH, CO, etc.; X = alkylidene, phenylene,

piperazino, etc.], useful as antiinflammatory, antiarthritic, antiedemigenic, antihypertensive agents and platelet aggregation inhibitors, were prepared Treatment of flurbiprofen [3,4-F(Ph)C6H3CH(Me)CO2H] with NaOMe followed by reaction with Br(CH2)4Br in DMF afforded I [M = 3,4-F(Ph)C6H3CH(Me)CO; A = B = O; X = (CH2)4] which showed the antiedemigenic activity of 0.8 vs. 1 for flurbiprofen.

L16 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 1996:163887 CAPLUS
DOCUMENT NUMBER: 124:201789
TITLE: Preparation of aryl nitrate ester compounds having antiinflammatory ans well as analgesic and antithrombotic activities
INVENTOR(S): **Del Soldato, Piero; Sannicolo', Francesco**
PATENT ASSIGNEE(S): Nicox Ltd., Ire.
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9530641	A1	19951116	WO 1995-EP1233	19950404
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2190087	AA	19951116	CA 1995-2190087	19950404
AU 9522156	A1	19951129	AU 1995-22156	19950404
AU 702662	B2	19990225		
EP 759899	A1	19970305	EP 1995-915185	19950404
EP 759899	B1	19990915		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
HU 75961	A2	19970528	HU 1996-3107	19950404
BR 9507634	A	19970923	BR 1995-7634	19950404
JP 09512798	T2	19971222	JP 1995-528615	19950404
AT 184589	E	19991015	AT 1995-915185	19950404
ES 2139199	T3	20000201	ES 1995-915185	19950404
RU 2145595	C1	20000220	RU 1996-123280	19950404
US 5861426	A	19990119	US 1997-737426	19970306
US 5780495	A	19980714	US 1997-902570	19970729
GR 3032078	T3	20000331	GR 1999-403169	19991208
PRIORITY APPLN. INFO.:			IT 1994-MI916 A	19940510
			IT 1994-MI1731 A	19940809
			GB 1993-20599 A	19931006
			WO 1995-EP1233 W	19950404
			US 1996-624508 A3	19960405

OTHER SOURCE(S): MARPAT 124:201789

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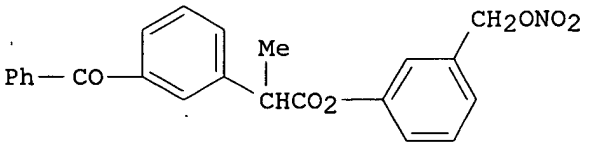

I

AB The title compds. AX1NO2 [A = R(COXu)t; t = 0, 1; u = 0, 1; X = O, (un)substituted NH or NR1c wherein R1c = alkyl; R = (un)substituted Ph, etc.; X = YO; Y = alkylene, cycloalkylene, oxyalkyl, etc.] (e.g., I), which inhibit cyclooxygenase, are prepared

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L14           14 SEA ABB=ON  PLU=ON  (L11 OR L12) AND (BLADDER OR INCONTINEN
                 C?)
L15           28 SEA ABB=ON  PLU=ON  L13 OR L14
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